

FOREWORD.

THE THESIS HERE PRESENTED EMBODIES A STUDY OF
TROPICAL ULCER AS SEEN IN LAGOS, NIGERIA.

VARIOUS FORMS OF TREATMENT ARE REFERRED TO ,
TOGETHER WITH A DETAILED ACCOUNT OF EXPERIMENTS
PERFORMED IN CONNECTION WITH THE AETIOLOGY OF
THE CONDITION.

THE STUDY HAS EXTENDED OVER A PERIOD OF TWO YEARS
DURING WHICH THE WRITER HAS BEEN STATIONED AT THE
MEDICAL RESEARCH INSTITUTE , LAGOS.

THE ARRANGEMENT IN CHAPTERS FOLLOWS A NATURAL
SEQUENCE AND A COMPLETE RECORD OF FIFTY CLINICAL
CASES HAS BEEN KEPT WHICH WILL BE FOUND IN A
CONDENSED FORM AS AN APPENDIX.

ILLUSTRATIONS OF CLINICAL AND EXPERIMENTAL ULCERS
TOGETHER WITH MICROPHOTOGRAPHS HAVE BEEN SPECIALLY
PREPARED. A LIST OF REFERENCES IS GIVEN.



CHAPTER ONE.

CLINICAL AND AETIOLOGICAL ASPECTS OF ULCUS TROPICUM.

A great deal has been written on the subject of tropical ulcer but the actual cause remains obscure and the disease continues to be of grave economic importance in this as in other tropical countries. It will be advisable first to define the term and discuss some points in the aetiology.

Definition and Symptomatology.

A typical ulcer as seen in Lagos presents the following characteristics:-

A round or oval ulcer with a regular not undermined rolled edge. The base consists of ragged necrotic tissue or adherent slough covered with a thick foul smelling purulent discharge, greyish in colour, and frequently blood-stained. In depth it always extends to the subcutaneous tissues though deeper structures may be involved. The surface diameter varies from one to several inches. The

surrounding skin is nearly always hyperpigmented and oedema of the adjacent parts is frequently marked. In most cases a single ulcer is found but multiple ulceration is not uncommon.

The majority of ulcers are situated on the lower limbs, particularly the lower third of the leg, ankle, and dorsum of the foot. They may also occur, though rarely, in other regions of the body mostly on exposed parts. Unusual sites seen by the author include the upper arm, buttock and scrotum.

Toe ulcers are not uncommon, Carini (1) in Brazil, described a "Phagedaenic ulcerative onychia" which he considered should be regarded as a special localisation of tropical ulcer.

Pain is a variable symptom and is often slight considering the extent of the ulceration.

From the foregoing description it is fairly obvious that the lesion corresponds with that of *Ulcus Tropicum* as given in the standard text-books on tropical medicine such as Castellani and Chalmers (2).

Adenitis of the lymph glands draining the affected area occurs but is usually mild. It should be mentioned that enlarged femoral and inguinal glands are found in almost every native irrespective of ulceration.

General effects are those of a toxæmia and may vary in degree from a slight constitutional disturbance to

marked emaciation and cachexia.

The following types of ulcer are met with - acute - sub-acute - chronic - recurrent and "mixed" ie, superimposed on other varieties of ulceration such as yaws, syphilis etc.

The acute type is in the nature of a rapidly advancing phagaenic process commencing, as do all tropical ulcers arising per se, as a small pruriginous papulo-pustule or bleb. Local pain and constitutional effects are marked. In the majority of cases the acute process subsides in a few days and passes into the sub-acute phase described above as the typical ulcer.

The sub-acute in its turn, if untreated, tends to develop into the chronic ulcer which is characterised by a slightly raised and thickened edge, a base composed of adherent slough or septic granulations and a general thickening of the surrounding tissues with often marked hyperpigmentation of the skin.

Such ulcers may present a rather "punched-out" appearance. Recurrent ulcers are all too common and frequently a patient is discharged from hospital as cured only to return in a short time with a fresh ulcer at the old site. Weakness of the scar and its consequent liability to injury from trauma too slight to

damage normal skin probably account for these cases. Tropical ulcer may also be found as a superimposed condition on ulceration of the skin due to other causes, particularly, in this country, yaws and syphilis. The diagnosis in such cases may be difficult and a tendency has developed amongst casual observers to classify all ulcers of the lower extremities in natives as "tropical". This aspect is dealt with more fully under the heading of differential diagnosis (vide infra). Photographs of clinical cases illustrate the variety and type of ulcer observed.

Complications and sequelae.

Byam and Archibald(3) observe that septicaemia or pyaemia may supervene. Such an occurrence has not been within the present writer's experience but it is interesting to note that Rosenow and Tunnicliffe (4) describe a fatal case of pyaemia due to an anaerobic polymorphic bacillus, probably *B. fusiformis*. Larson and Baron (5) report a case in which the fusiform bacillus was isolated from the blood stream. In the Annual Medical Report Nigeria (6) an account is given of a case of tropical ulcer in which death ensued. From the findings at autopsy it would appear that the condition was a toxæmic and not a septicaemic one. Further reference will be made to this case. Rarely the ulcer takes on a virulent phagædænic

character with destruction of muscles, tendons and even bone.

A scar always remains to mark the site of ulceration and deformity may sometimes result from cicatricial contraction in bad cases.

Diagnosis.

The diagnosis is made on the clinical appearance and bacteriological examination . Occasionally a biopsy and histological investigation may be of help.

It has been found in Lagos that examination of the secretion by the dark-ground method and by stained smears invariably reveals the presence of spirochaetes and fusiform bacilli, usually in abundance.

Kersten(7) in contrasting the tropical ulcer of German New Guinea with the African type mentions that although the fuso-spirillary combination seems to be the usual finding in the latter such has not been his experience while investigating the former.

Roy(8) gives his findings in repeated examinations of smears from 156 cases of Naga Sore in Assam as follows,

- (1). Fusiform bacilli in 59.
- (2). Spirochaetes and fusiforms in 4.
- (3). Spirochaetes alone in two.
- (4). Negative findings in 91.

Fox(9) also examining smears from Naga sores found enormous numbers of bacilli, mainly fusiform, and in some cases spirochaetes. He states that Naga Sore

corresponds to tropical ulcer as described by Castellani and Chalmers. This statement is borne out by Roy's description of the sore.

(10)
Burnie, in Northern Nigeria, gives the following results from an unselected series of untreated ulcers.

No. of cases	133.
Spirochaetes and fusiform bacilli....	107.
Fusiform bacilli alone.....	7.
Spirochaetes alone	2.
Neither	17.

It should be noted that the last three writers did not make use of the dark-ground method^{of} examination .

Differential diagnosis.

The various conditions are discussed in the order of their importance in Nigeria.

Yaws.

In this disease the earlier lesions tend to be granulomatous rather than ulcerative and are usually multiple. Careful examination frequently reveals the *Treponema pertenue* which is quite unlike the spirochaetes found in tropical ulcer. The tertiary or late ulcerative lesions of yaws are generally multiple, irregular and deep or large and fungating.

Tropical ulcer, unlike that of yaws, is most frequently met with on the lower limbs. The former condition may be superimposed on an ulcerative framboesia lesion though, in the experience of Castellani and Chalmers

the reverse is much more common.

It was fortunately possible to visit Benin City , an endemic centre of yaws, and to obtain photographs of the later lesions.

Syphilis.

Confusion should not arise as tropical ulcer lacks the characteristic features of late syphilitic ulceration. The failure to respond to anti-syphilitic treatment on the part of tropical ulcer is of further help in the diagnosis. The Wassermann test and its substitutes the Kahn and Sachs-Georgi are of little value since a positive result is obtained in a high percentage of all hospital cases in Lagos. Ramsay(11), working in Calabar examined 2,531 sera by the Sachs-Georgi test and found 56.5% positive. Of 600 hospital in-patients over eighteen years of age he found that no less than 65% gave a positive reaction . In Lagos the Kahn test has been performed on a number of juveniles suffering from tropical ulcer with negative results.

Traumatic lesions.

The appearance together with the definite history of recent injury are in themselves sufficient to establish the diagnosis. That such injuries frequently become infected with the aetiological agent of tropical ulcer must not be forgotten.

Streptococcal ulceration.

Such lesions, common in Lagos particularly in juveniles, are characterised by multiplicity, shallowness, accompanying bleb formation and rapid healing under simple measures. They have been described by Smith(12) some of whose photographs , together with others of cases which have come under my personal observation, are here reproduced.

Guinea-worm.

Some tropical ulcers may owe their origin to guinea-worm infection. In early cases the diagnosis is self-evident from the presence of the worm . The condition is extremely prevalent in Nigeria.

Chigoes.

The ulcers caused by this parasite(Tunga penetrans) are usually multiple and commonly involve the toes and plantar aspect of the foot . As in the case of guinea-worm they may develop later into tropical ulcer.

Malignant ulceration.

This is rare among natives but the possibility of malignant changes occurring in tropical ulcer must be borne in mind.

Leprosy.

Trophic ulcers of the perforating type may be met with but the diagnosis can usually be made without difficulty as other signs and symptoms of the disease are also present.

Varicose ulcers.

The presence of varicose veins in most cases and the superficial irregular character of the ulcers establish the diagnosis.

Tubercular ulcers.

These are of very rare occurrence, especially so upon the legs. They develop slowly and in appearance are unlike *Ulcus Tropicum*.

Oriental sore.

The parasite of oriental sore has not yet been found in Lagos. A chronic sore may simulate a chronic tropical ulcer but is usually smaller.

Veldt sore.

This condition does not appear to have been recorded in Nigeria. In early cases the isolation of the Klebs-Loeffler bacillus and in chronic cases the typical rounded, punched-out appearance serve to make the diagnosis.

Ulcers due to native medicine.

The remedies employed by the native medicine-man are varied and strange. There is no doubt that some of them when applied to minor skin lesions may cause a devitalisation of the tissues readily leading to secondary infection and ulceration. The native doctor is naturally reluctant to explain the composition of his medicines to a European.

Amoebic ulcer.

Amoebic ulceration of the skin is said to occur but because amoebae are found it does not necessarily follow that the condition is due to their presence. They may well be coprozoic types and the only true criterion is definite proof of their pathogenicity by culture and subsequent animal inoculation. McCulloch(13) quotes Kofoid, Boyers and Swezy in connection with amoebic skin ulceration.

Ulcers of mycotic origin.

These include blastomycosis, sporotrichosis, acladiosis, mycosis fungoides, actinomycosis and mycetoma. The first four are at present unknown in Lagos, actinomycosis is extremely rare and the clinical appearance of mycetoma is quite unlike tropical ulcer. The diagnosis in all these conditions is dependent on naked-eye appearances and the finding of the characteristic fungus.

Malarial ulcer.

Cross(14) has described "malarial ulcers" in central Africa. His description corresponds to that of tropical ulcer and he considers malaria as a possible reducing agent from a constitutional point of view.

Prognosis of tropical ulcer.

The ulcer, if untreated, shows very little tendency to heal spontaneously or, at best, healing is extremely slow.

Aetiological factors.

Geographical distribution.

Tropical ulcer is found throughout the tropics and sub-tropics and synonyms such as Mozambique Ulcer, Aden Ulcer, Cochin Sore and Yemen Ulcer are derived from the districts in which it is prevalent. Manson-Bahr(15) mentions the condition as being particularly common in hot damp climates. In Nigeria, however, it appears to occur with greater frequency in the dry sandy regions of the Northern Provinces than in the humid low-lying districts of the coastal belt. Burnie(10) states that at least 95% of the skin ulcers met with in Kano and the surrounding districts are "Ulcus Tropicum".

Seasonal incidence.

Assmy and Kryitz(16) find that tropical ulcer becomes most severe with high temperatures and enters upon a resting phase with cooler temperatures. Adams(17) working in Syria considers it a dry weather disease flourishing throughout the summer drought and never beginning in the rainy season. In the report of the Pasteur Institute, Shillong(18) Naga Sore is described as being prevalent during the monsoon. Roy(8) investigating Naga Sore in Assam, found that the season of onset varies with the place but that in most

localities it appeared after the first shower in the hot months with a maximum incidence in July during the heavy rains. Burnie(10) in Northern Nigeria, notes that there is a rise during the later months of the rainy season with regard to the number of cases attending for treatment. In the Lagos district more cases are seen at the hospitals and dispensaries during the rains. There is a marked falling off, in the Author's experience, during the last two months of the dry weather.

Epidemiology.

The occurrence of tropical ulcer may, at times, reach epidemic proportions . Adams(17) records an epidemic which commenced in Syria in 1916 and reached its height three years later. Apostolides(19) and Gerschon(20) have written of an outbreak in Palestine in 1919 to 1920. Manson-Bahr(15) quotes Lloyd Patterson who described an epidemic which "Swept like a plague up the whole of Assam". Such widespread epidemics do not appear to have been recorded in Nigeria though smaller outbreaks amongst troops, labour gangs etc. are not uncommon. The disease is endemic throughout Nigeria but in the present state of development of the country accurate estimation of its incidence is not possible. All one can say is that it is extremely prevalent.

Race.

Race.

The native inhabitants of the tropics and sub-tropics are almost the only sufferers from this disease. Cross(14) studied 29 cases in Europeans in British Central Africa and Edge(21) notes that ulcers similar to Ulcus Tropicum occur amongst Europeans in the Cocos and Perim. In Nigeria Europeans are rarely if ever affected. No case has come under the writer's notice during the past four years.

Class.

The majority of observers agree that the poorer classes of the community are by far the most affected. It is probably largely a question of occupation, the manual labourer being not only lower in the salary scale but more liable to infection from the nature of his work. It is worthy of note that the only better class natives in Lagos who suffer from tropical ulcer are school children, the majority of whom still go barefooted. Adams(17) described an epidemic in Syria in which the ulcers invariably occurred on the exposed parts of the poorer people.

Sex.

Castellani and Chalmers(2) observe that the disease is much more common in men than in women and that is the opinion of most writers. Roy(8) working in Assam gives

the sex incidence of Naga Sore as 65.7% males and 34.3% females . Smith(6) in Lagos found 50% in males . The present writer, also working in Lagos, notes 76% of the ulcers as occurring in males. Wolbach and Todd(22) in the Gambia found a greater preponderance amongst women and children.

Occupation is probably the most important factor in determining the sex incidence.

Age.

Roy(8) in Assam, gives the age incidence as 99.6% adults. Castellani and Chalmers(2) state that *Ulcus Tropicum* is much more common in adults than in children. Burnie(10) in Northern Nigeria, finds children and the aged to be remarkably free but mentions that in Lagos the ulcers are not uncommon in the young. My own observations, made in Lagos, agree with those of Burnie and I have found a markedly high percentage (44%) occurring under the age of eighteen years. This percentage is probably due to the more developed state of Lagos where medical inspection of school children has recently been organised with a consequent increase in attendance at the Government dispensaries and hospitals .

Immunity.

Roy(8) from his investigations of Naga Sore found

that an attack of the disease conferred no immunity. The present writer's study of clinical tropical ulcer and the results of experimental inoculations fully confirm the lack of immunity. It is possible, if one considers the theory of a specific organism, to suppose the existence of different strains. In that case immunity may be developed to one strain and the patient still be open to infection with another.

Natural transmission of the disease.

The possibility that insects may be concerned in the transmission of the disease has received consideration from various writers. Castellani and Chalmers(2) state that in Ceylon patients often give a history of an ulcer developing at the site of a leech bite, but they point out that Prowazek, who examined many leeches in Java, never found spirochaetes of the type seen in tropical ulcer. Fox(9) in Assam, drew attention to the fact that an epidemic of Naga Sore is associated with a plague of small flies identified as *Siphonella funicola*. Hall Wright(23) proved that Naga Sore can be passively transmitted by this fly. He allowed the insects to feed on a case and then transferred them to his own arm, a typical lesion developing later. Roy(8) also attempted transmission experiments with *Siponella funicola* but without success. He found that the spirochaetes and fusiform

bacilli were readily taken into the gut by the flies but that there was no evidence of their multiplication there although a change of shape occurred.

Onorato(24) notes that flies may be important carrying agents. Apostolides(19) thinks that mosquitoes play a part in the transmission and finds strong support for his theory in the fact that tropical ulcer is common in those parts of the world where malaria is also endemic. Nothing, however, has yet been put forward to disprove the opposing theory of mechanical transmission.

Cross(14) records an interesting case of auto-inoculation . A native had a typical sore on the leg which, when he adopted a squatting attitude, touched a small abrasion on the opposite foot. He was encouraged to do this and in seven days the inoculated spot had developed into a sore exactly like the original. Peters(25) mentions two cases of injury to the hand due to striking a man on the teeth. The resultant lesions were swollen and oedematous with a foul discharge. In one, fusiform bacilli and streptococci were found but no spirochaetes. In the other, smears showed almost pure spirochaetes and fusiform bacilli.

Roy(8) investigating Naga Sore in Assam is of the opinion that the disease is not contagious. In five of

his cases repeated examination failed to show fusiform bacilli but when the patients stopped treatment, pulled off their dressings and walked about in the mud infection with this organism took place. He therefore suggests that wounds become infected with fusiform bacilli from the soil, some soils being more richly charged than others.

Bouffard(26) considers it possible that the fusospirochaetal symbiosis enjoys a saprophytic existence in the soil. Apostolides(19) differs from Roy as regards the contagious character of the disease. He(Apostolides) states that direct contagion from man to man is shown by the fact that patients suffering from wounds and occupying beds next to cases of tropical ulcer almost invariably contract that condition.

Two interesting cases are recorded by this writer. The first was one of direct infection in a nurse whose forearm was accidentally scratched with a knife which had previously been used to incise an ulcer. A typical lesion developed in spite of immediate antiseptic treatment of the wound. The second case was that of a woman who was bitten on the breast by a man, a characteristic ulcer developing at the site of the injury. Her assailant was examined later and found to be suffering from ulcero-membranous stomatitis, fusiform bacilli and spirochaetes being present in abundance.

The present writer, while aware that much remains to be discovered concerning the natural transmission of tropical ulcer, is of the opinion that various factors operate from time to time. Under the crowded and insanitary conditions which still prevail in the large towns of such a country as Nigeria direct infection from man to man by actual contact of small wounds with the ulcers or their foul dressings is probably common. The supposition that the house-fly plays its part in mechanical transmission does not seem unreasonable considering its habit of feeding on open sores whenever the opportunity arises. Previous reference has been made to the work of Cross(14) who proved that auto-inoculation can take place.

The history of some minor injury as the starting point of tropical ulcer is almost invariably given by patients in this country. It is therefore not improbable that infection with the aetiological agent, present perhaps in the dust or soil, is thus brought about.

The host, if there is one other than man, is unknown.

Predisposing causes.

Trauma.

There is little doubt that some minor injury to the skin is the most usual starting point of a tropical ulcer. It is the exception, in the writer's experience, for a patient, on being questioned as to the history, to put forward any other reason than trauma for his ulcer. The native who contracts Ulcus Tropicum is usually of the poorer labouring class, goes barefooted and is not too scrupulous as to his personal cleanliness, and these factors must be added to the traumatic one. To quote Manson-Bahr(15) " The feet and legs, being most exposed to injury, are the most frequent location of this form of ulceration".

Diseases of the skin.

Any skin disease causing a loss of continuity of the epithelium may conceivably provide a favourable nidus for infection with tropical ulcer. Castellani and Chalmers(2) and Roy(8) make particular mention of scabies as a predisposing cause.

If skin disease were a common factor in the predisposition to tropical ulcer one would expect the lesions to be less confined to the lower limbs. It is worthy of note that the only two cases of arm ulceration seen by the writer occurred at the site of recent

anti-variola vaccination.

Climate.

According to Castellani and Chalmers(2) a hot damp climate is said to have a predisposing influence as the ulcers are more frequent in the hot rainy season and in marshy lowlands. As previously mentioned under "Geographical distribution" and "Seasonal incidence" *Ulcus Tropicum* in Nigeria is more commonly met with in the dry sandy Northern Provinces though the maximum incidence both in the North and South of the country occurs during the rains.

Debility.

Certain diseases are so prevalent in the tropics that it is exceptional for the native inhabitants to go through life without having had one or more of them. In Southern Nigeria malaria, dysenteries and diarrhoeas, gonorrhoea, syphilis, yaws and helminthic infections are all extremely common and there can be no doubt that they cause much debility amongst the population.

Butler(27) working at the African Hospital Lagos, examined blood films from 3,385 individuals and found malaria parasites, mostly subtertian, in 30%.

Out of 527 faecal examinations *ascaris* ova were present in 71% and *ankylostome* ova in more than 50%.

Ramsay(11) at the Calabar native hospital, carried out

stool examinations for parasites and ova in 1583 cases with a positive result in 92.1% . Ankylostome infection was 62.1%.

Debility implies lowered resistance to infection hence it is not unreasonable to suppose that the above-mentioned diseases pave the way for such affections as Ulcus Tropicum. That the latter process is a reaction to an organism having slight powers of invasion is an explanation put forward by Wolbach and Todd(22) who find support in the fact that the ulcers are usually solitary and on regions exposed to trauma.

The writer's own attempts at experimental inoculation are additional evidence in favour of this view.

Although debility must be considered as an important factor predisposing to tropical ulcer it is not a "sine qua non" of the disease. A number of cases of Ulcus Tropicum have been observed in Lagos to occur in healthy well-nourished school children belonging to the more prosperous section of the community.

Dietetic deficiency.

There is a tendency at the present time to stress deficiency in diet as a causative factor in various diseases among which tropical ulcer must be numbered. Edge(21) in Cocos and Perim, found that this form of ulceration occurred in Europeans only in areas where the ordinary diet was unavoidably restricted.

A free supply of fresh vegetables and fish reduced the trouble in Cocos by 50%. Manson-Bahr(15) notes that the blood calcium is said to be much diminished in this disease as a result of deficient dietary. It is of interest in this connection to refer to the work of Green and Mellanby (28) who have shown that animals reared on a diet deficient in vitamine A all die with infective or pyogenic lesions.

McCulloch(13) working in Northern Nigeria, made a biochemical analysis of the blood of natives in Katsina and finds a high blood sugar but no glycosuria, calcium deficiency and a low blood urea. He states that the native dietary shows a high carbohydrate predominance but is low in protein and salts. He reaches the conclusion that tropical ulcer is conditioned by a chronic semi-starvation of the vast majority of the population and the entrance of any mildly pathogenic organism, and makes the rather sweeping statement that "Tropical ulcer is a dietetic ulcer and the question of causative organisms need not be considered at all".

Young(29) in a criticism of this author's views points out the importance of studying early cases of *Ulcus Tropicum*. He considers that the initial acuteness and the subsequent slowing down of the rate of invasion in the course of a week or so are the reverse of what one

expects to find in a deficiency disease. He favours the theory of a specific organism and finds support in the beneficial results of surgical treatment in early cases, whereby the lesion is reduced to the state of a clean surgical wound which shows no tendency to revert to a phagaedenic condition. In the opinion of the present writer dietetic deficiency is an important predisposing cause of tropical ulcer but is not by any means the sole factor in the aetiology. The diet of the native of Southern Nigeria undoubtedly contains an excess of carbohydrates but, compared with that of the Northern native, it is probably much more varied. In many districts fruit, vegetables and fresh fish are plentiful during the greater part of the year. It is true that the majority of cases of tropical ulcer seen in Lagos are in poor physical condition but the starved and emaciated patients are usually found to be natives of the Northern Provinces. Most of them have found their way on foot from their distant homes and, travelling often without visible means of sustenance, arrive in Lagos in a state of physical exhaustion. In the absence of information which could be derived from a strict dietetic survey of the Southern Provinces it would be unwise to make a dogmatic statement but, as

far as conditions in Nigeria are concerned, it appears that the dietetic factor is of greater importance in the North than in the South.

Organisms.

The various organisms met with and their possible incrimination in the cause of tropical ulcer are discussed in the chapter on Bacteriology.

End of Chapter One.

CLINICAL TYPES OF TROPICAL ULCER.



CLINICAL TYPES OF TROPICAL ULCER.



CLINICAL TYPES OF TROPICAL ULCER.



Fatal case. (See page 46).



CLINICAL TYPES OF TROPICAL ULCER.



Superimposed upon
a vaccinia lesion.



CLINICAL TYPES OF TROPICAL ULCER.



Marked sloughing of skin.



Chronic case. Note the marked thickening and induration of the tissues.

DIFFERENTIAL DIAGNOSIS.



Streptococcal ulceration in a child aged five years.



Varieties of chronic framboesial ulceration.

DIFFERENTIAL DIAGNOSIS.



Guinea-worm ulcer.



"Mixed" type of ulceration.

CHAPTER TWO.

TREATMENT.

A. Prophylaxis.

There is great truth in the old adage "Prevention is better than cure" and to no disease is it more applicable than Ulcus Tropicum. It is obvious, however, that the possibility of introducing prophylactic measures amongst the general population of the tropics is at present remote, and it is only in the case of communities under definite supervision and discipline such as soldiers, police, labour gangs, schools and prisons that steps towards prevention are likely to be of any avail. Protection from trauma must be the first consideration and may be effected, at any rate amongst soldiers and police, by the wearing of suitable apparel such as sandals, puttees etc. All minor injuries must be reported immediately and appropriate treatment adopted. Regular and frequent medical inspection is of importance and facilities for bathing should be available. The question of diet requires

consideration and attention must be paid to variety as well as sufficiency. The possibility of contagion must be borne in mind and whenever feasible sufferers from the disease must be isolated.

B. Curative measures.

The multiplicity of methods used in the treatment of tropical ulcer is of itself an admission of failure to discover a specific remedy. The problem, however, is a very real one and it is felt that a review of the available literature and an account of the author's own experience would not be out of place in this thesis.

It has been considered advisable first to refer briefly to the principle measures and then to enter upon a discussion of their relative values.

The following lines of treatment are those most generally used. They may be employed individually or in various combinations.

- (1) Rest in bed and the usual hospital diet combined with a simple local dressing such as saline.
- (2) Special dietary with a view to supplying possible vitamines and other defects, eg. Cod-liver oil.
- (3) Internal remedies :-
 - (a) Tonics etc.
 - (b) Drugs of alleged specific effect such

as arsenic, antimony and bismuth administered by the intravenous or intramuscular route.

(4) Local therapy:-

(a) Dressings. Drugs used in solution include acriflavine, picric acid, perchloride of mercury, Friar's balsam, balsam of Peru, magnesium sulphate, methylene blue, potassium permanganate, arsenicals, lactic acid, carbolic acid, formalin, normal saline, eusol and various others.

Medicaments used in the dry state are tartar emetic, iodoform, Vincent's dressing, normal serum, cyanide, boracic acid, calomel powder.

Ointments of bismuth, mercury and protargol have been employed.

(b) Baths. Various antiseptics may be used , chief amongst which are cyllin and eusol.

(c) Irrigation. Antiseptics of the chlorine group ie. Dakin's solution, eusol and eau de Javel are the most frequently employed.

(d) Cauterisation. The thermo-cautery.

(e) Measures to improve the local circulation, for example strapping , posture etc.

(f) X-rays and ultra-violet light.

(5) Vaccines.

(6) Surgical measures:- scraping, skin-grafts etc.

(7) Concomitant diseases such as yaws, syphilis etc.

require appropriate treatment.

Discussion.

The various methods enumerated above will be considered, as far as possible, in the order given. It should be understood that the majority of cases seen by the author at the African Hospital, Lagos, were treated by the clinicians in charge of the wards and it was by their courtesy that he was permitted to observe the effects of several different methods. A limited number of cases were treated personally during the period devoted to the present study of tropical ulcer and also during a former tour of duty in Nigeria as Medical Officer in charge of an up-country station.

(1) Rest in bed etc.

Smith(6) in Lagos, records a rapid clearing up of the condition in patients kept at rest and treated with simple dressings such as saline. Byam and Archibald(3) recommend rest, good hygienic surroundings and a liberal diet. The present writer, whilst attempting the culture of organisms from the lesions found it necessary to keep some of the patients in bed for a few days on sterile water dressings and it was noticed that in several of them

the condition rapidly improved. The difficulty in treating tropical ulcers among out-patients further emphasises the importance of rest in bed under hospital regime.

(2) Special dietary.

Burnie(10) in Northern Nigeria, has found no improvement in the rate of healing in patients treated with a view to supplying vitamine deficiencies. When considering the question of diet as a predisposing cause reference was made to Edge(21) who noted that a supply of fresh vegetables and fish halved the incidence of tropical ulcer amongst Europeans in Cocos. Manson-Bahr(15) recommends fresh vegetables and lime juice. It is only rational, in districts where the diet has been proved deficient in vitamins or other factors, to attempt to remedy such defects in the hospital treatment of tropical ulcer.

(3) Internal remedies.

(a) Tonics etc. Every effort must be made to correct debility and improve the general condition of the patient and herein tonics are of value. Calcium may be given in view of its deficiency in the blood in this disease. Manson-Bahr(15) recommends opium in full doses both for its analgesic effects and for its special action on the

phagedaenic process.

(b) Drugs of alleged specific effect administered by injection.

Arsenical compounds. There has been much controversy as to the specific effect of salvarsan and its derivatives in the treatment of tropical ulcer.

Werner(30) refers to a paper by Schüffner who claims good results from intravenous salvarsan. This is contrary to his own experience. Assmy and Kryitz(16) consider that salvarsan acts specifically.

Rousseau(31) using novarsenobenzol, finds the intravenous method more certain, simultaneous intravenous and local medication being, in his opinion, costly and unnecessary. Bouffard(32) on the contrary, states that intravenous neosalvarsan is practically inactive in this condition. This view is supported by Smith(6) who mentions fifteen cases treated at the African Hospital, Lagos, by full courses of N.A.B. ie. four to six injections of 0.6 grammes each. There was no improvement, the ulcers either remaining stationary or definitely retrogressing. Gerschon(20) in Palestine and Kersten(7) in German New Guinea also found intravenous salvarsan of no benefit.

The present writer has observed a considerable number of cases treated by intravenous injections of neosalvarsan, each patient receiving a total of not less

than three grams of the drug. The results fully confirm the observations of the last four authors as to the inefficacy of this mode of treatment. Injections of salvarsan or its derivatives are of no avail except in ulcers of "mixed" type ie. where tropical ulcer is superimposed upon lesions of syphilitic or fraemboesial origin. The apparent specific effect of the drug in such cases may lead to erroneous statements in the literature as to the value of this form of treatment.

Antimony. Kervram(33) records thirteen cases treated by intravenous injections of tartar emetic, the ulcers healing after 22cg. had been given. It seems probable that these lesions were not true Ulcus Tropicum as, in the present writer's experience, this drug has no specific effect.

Bismuth. As with the injection of arsenical compounds the beneficial effects claimed for bismuth are probably the result of its use in mixed cases where there is an underlying syphilitic or fraemboesial element.

Houssiau(34) reports a case of tropical ulcer of three and a half months duration which cleared up after three injections of bismuth succinate. Local applications of bismuth hydroxide were used concurrently.

Intramuscular injections of "Bivatol" have been tried in a few cases in Lagos but produced no effect on the ulcers.

(4) Local therapy.

(a) Dressings. Solutions of acriflavine 1 in 1000, perchloride of mercury 1 in 1000, magnesium sulphate 25% , potassium permanganate 1 in 500, picric acid 1%, eusol and Friar's balsam have all been used in the treatment of tropical ulcer at the African Hospital Lagos. No special advantage can be claimed for any one of these though the beneficial effects of eusol in ulceration involving bone deserves mention . Byam and Archibald(3) recommend perchloride of mercury, James(35) compresses of magnesium sulphate, and Roy(8) potassium permanganate. Kersten(7) has found balsam of Peru of benefit and Kervrann(33) mentions 3% methylene blue as a useful local application.

Simple dressings of saline, combined with rest, have often a marked effect in clearing up these ulcers. Lactic acid, carbolic acid and formalin have been used on account of their penetrating caustic action. Gerschon(20) found pure lactic acid the best remedy during an epidemic in Palestine. Bouffard(26) refers to Fontoynt as having recorded good results with the same drug.

Manson recommended swabbing the ulcers with pure carbolic acid. This remains one of the most effective

methods in checking the phagedaenic process and has been used by the present writer in a number of cases with success. Boucher(36) describes 14 cases rapidly cured by the application of "Formol" (40% formalin) followed by bismuth dressings. Manson-Bahr(15) states that this mode of treatment appears to be the most successful. The present writer has recently tried it in 6 cases at the African Hospital Lagos. The results were disappointing as, although the phagedaenic character of the ulcer is abolished, the surface appears to be devitalised by the formalin rendering it an even more favourable soil for the multiplication of pyogenic organisms. As a consequence further treatment was troublesome and healing extremely slow. It should be mentioned that all the cases were in-patients and therefore under the best possible conditions.

The local application of salvarsan or its derivatives.

Bouffard(32) finds a specific remedy in 3% solution of neo-salvarsan. This form of treatment is also recommended by Goldberg(37) and Onorato(24), the latter advocating glycerinated N. A. B. Gerschon(20) on the contrary considers local neo-salvarsan not only useless but definitely irritating.

As there seemed to be some claim to specific effects from these drugs the method was given a trial recently in Lagos by the present writer. The technique adopted

and the results obtained are recorded here in a condensed form:-

Preparation . Neosalvarsan in fresh solution.

Strength. (a) For patients 8 years and over
4% in sterile distilled water.
(b) For patients under 8 years
2% in sterile distilled water.

Technique. The secretion was removed by swabbing the ulcer with cotton wool tampons wrung out of sterile water. The solution was then applied on plain lint brought into intimate contact with the base and edges. The ulcer was dressed once daily.

No. Of cases treated. 18 unselected as to age or sex. Fifteen were in-patients and three out-patients.

Ages varied from $1\frac{1}{2}$ to 29 years.

Average No. of daily applications. Five.

Maximum No. on successive days. Eight.

Minimum No. " " " " " " . Four.

Subsequent treatment. (1) Dry dressings of boric powder in cases where healing was rapid.

(2) Eusol packs and surgical measures in two cases involving bone.

(3) Red lotion or scarlet red ointment in cases tending to become indolent. The latter proved to be the more efficacious.

Results. In 16 cases there was a rapid cessation

of the phagedaenic process , the condition being transformed in three or four days into a simple lesion covered with a brown scab. This scab separated later leaving, in the majority of cases, a clean granulating surface. The remaining two patients appeared to be unduly sensitive to the drug and treatment was abandoned owing to the local irritation.

The ulcers, although rapidly reduced to a simple state, healed slowly taking from three weeks to three months. The average duration was about seven weeks in uncomplicated cases.

Complications. Two cases required subsequent surgical treatment to remove necrotic bone. Two others broke down when almost healed to form a superficial ulcer with a serpiginous edge and a base of well defined granulations which tended to bleed readily. Markedly haemolytic streptococci were recovered by Griffon's technique from these ulcers. Pure cultures of the organisms were inoculated, in the first instance, intra-dermally into guinea-pigs and produced mild pyogenic lesions. Human volunteers were afterwards inoculated in the same way and in these definite abscess formation occurred. Since these experiments were performed similar ulcers, unassociated with *Ulcus*

Tropicum, have been seen occasionally among out-patients at the African Hospital Lagos. All were situated on the lower limbs and in the majority of cases were single. Haemolytic streptococci have been isolated from these also.

Remarks. Local application of neo-salvarsan solution has given good results in a number of cases of tropical ulcer in so far as the phagedaenic process has been quickly arrested. The fuso-spirochaetal association disappeared early from the lesions. Healing, however, was slow and this form of treatment cannot be said to lessen the stay in hospital to any appreciable extent. The high cost of the drug renders its use on a large scale prohibitive. The solution must be freshly prepared and treatment carried out only by trained dressers.

Medicaments used in dry or powdered form.

Tartar emetic in powder form is regarded by Mei(38) as efficacious treatment, particularly against the spirochaetes. Iodoform has been tried in Lagos but is of no special benefit. Saporte(39) records good results and rapid epithelialization with Vincent's dressing. The formula is:- Hypochlorite of lime 10 parts, powdered boracic acid 90 parts. It is interesting to note that Amaral(40) has used normal dried serum in the treatment of phagedaenic

ulcers. The lesions improved rapidly and there was complete destruction of the fuso-spirillary association. Howard(41) in Nyassaland, recommends dusting with cyanide powder. Powdered boracic acid is useful after the phagedaenic process has been stayed by other means. Calomel powder has been tried recently on a limited number of cases at one of the Government Dispensaries in Lagos with moderately good results.

Ointments.

Previous reference has been made to Boucher and Manson-Bahr in connection with treatment by formalin. Both these authors recommend subsequent bismuth dressings. It has been found in Lagos that bismuth per se, used locally, has little action. The same applies to ointments containing mercury. Castellani and Chalmers(2) advise 5 to 20% protargol ointment after cleansing the ulcer with a solution of perchloride of mercury.

(b) Baths. Foot baths containing warm antiseptic solutions such as eusol and cyllin are particularly useful in large ulcers with a copious foul-smelling discharge. The baths are usually followed by one of the foregoing medicaments. Hot boric fomentations are also of value in the above.

(c) Irrigation. Blondin(42) finds marked improvement by continuous irrigation for eight hours a day with "Eau de Javel", a solution containing chlorine. Rousseau(31) considers Dakin's solution good but troublesome. The latter statement, in the opinion of the present writer, aptly summarises treatment by irrigation.

(d) Cauterisation. Normet(43) first powders the ulcer with iodoform and then uses the thermo-cautery so as to make a black crust covering the whole area. On top of this a wet dressing of "Water of Alibour" is applied. He states that this treatment cures in from one to three weeks. Bouffard(26) on the contrary, considers the thermo-cautery dangerous as it excites the infection.

(e) Measures to improve the local circulation. Elevation of the affected limb may prove of value in hospital treatment. Good results are said to be obtained from strapping and saline dressings, the part being kept at rest.

(f) X-rays and ultra-violet light. Manson-Bahr(15) suggests that X-rays should be tried when available. The Radiologist to the African Hospital, Lagos, has treated many cases by X-rays and ultra-violet light. He finds a temporary beneficial

effect with a tendency to relapse on cessation of treatment. General irradiation of the body is of little use.

(5) Vaccines.

Van Nitsen and Walravens(44) attempted vaccine treatment in two hundred cases and found it useless. The mixed vaccine was made from an anaerobic culture of ulcer material in ascitic fluid. Pons(45) used a diluted culture of a polymorph spirillum isolated by himself from the buccal cavity. This is said to cut short all fuso-spirillary infections though its effect on skin ulcers is not so rapid as it only arrests the phagedaena. Smith(6) in Lagos, records improvement in chronic cases with autogenous vaccines of *Ps. pyocyanea*. He considers, however, that the amelioration may be due to protein shock. Vaccine treatment may prove of great benefit if it is possible to isolate in culture the causal organism.

(6) Surgical measures.

Thorough scraping of the ulcer with the Volkmann's spoon, the edges being trimmed with curved scissors, is often effective in cutting short the phagedaenic process. Even if the raw surface is subsequently re-infected it but rarely reverts to its former condition. The chief objection

to this form of treatment is that it leads to excessive cicatrisation. Attempts may be made to obviate this by skin grafts. It may well be that thorough removal of the lesion by scraping would prove effective in the very early ulcer or pre-ulcerative bleb, but cases at this stage seldom appear at the hospitals and dispensaries.

Other surgical measures include removal of sequestra and even amputation in advanced cases.

Remarks on treatment.

It is not possible in the light of present knowledge to evolve an efficacious standard treatment for Ulcus Tropicum, however desirable it may be to do so.

These ulcers are extremely variable in their reaction and, in considering treatment, due attention must be paid to the type involved ie. acute, chronic, etc. Sufficient indication has already been given in this chapter as to which methods are considered efficacious and which are definitely of no avail, and it only remains to outline briefly what appears to be the most satisfactory treatment from the present Writer's own experience in a limited number of cases.

The patient usually presents himself when the initial

acute process is slowing down or when the ulcer has become chronic in character. In the first type of case he ought, whenever possible, to be kept at rest and the affected limb elevated. Local treatment should consist of thorough removal of the secretion daily followed by a simple dressing of saline or a mild antiseptic such as acriflavine 1 in 1000. If the ulcer does not show rapid improvement recourse must be had to some method, such as the local application of neo-salvarsan or swabbing with pure carbolic, which will stay the phagedaenic process. Once the ulcer has been reduced to a simple condition treatment follows the usual lines aiming at the promotion of rapid healing. Mention has already been made of the beneficial effects of scarlet red ointment on epithelialization.

In the second (chronic) type rest in bed is also indicated. Treatment by local antiseptics is likely to prove extremely ^{tedious} and it is probably best to scrape the ulcer thoroughly and remove the thickened edge with the curved scissors. A skin graft, if successful, will reduce the time of healing and prevent deformity from excessive cicatrisation. General measures such as a liberal diet, tonics etc. are indicated in every case. Appropriate treatment is required for any concomitant affection such as

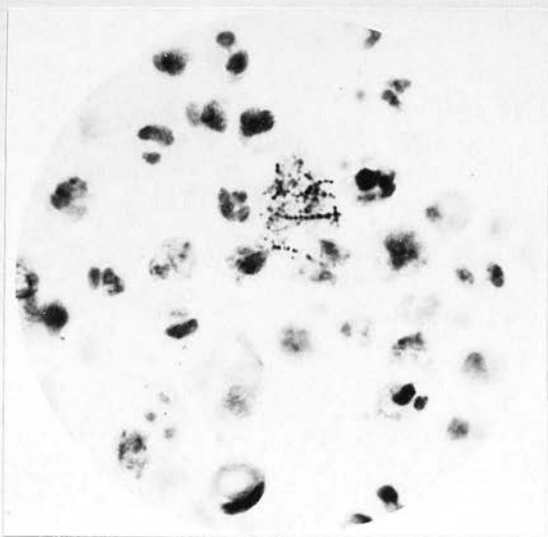
yaws, syphilis, malaria, helminthiasis etc.

End of chapter two.

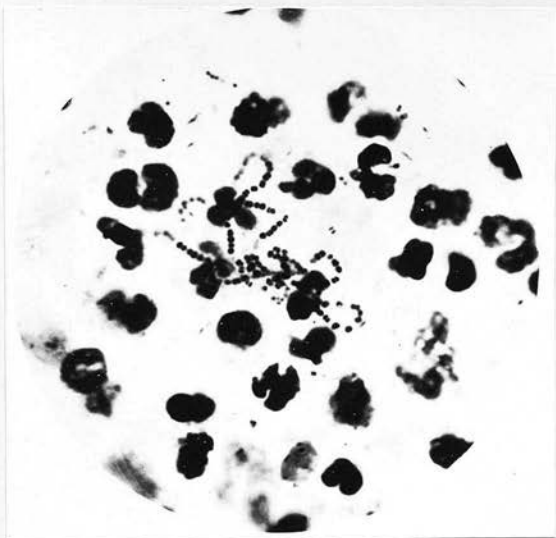
STREPTOCOCCAL INFECTION IN TROPICAL ULCER.



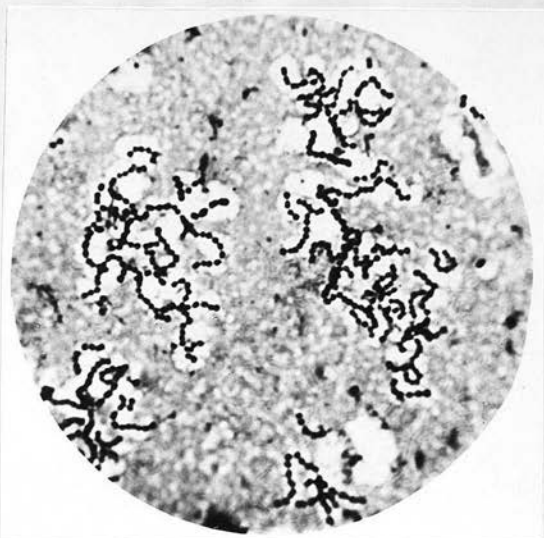
Type of lesion
(See page 35)



Smear from ulcer
showing short chains.



Smear from experimental
abscess.



Streptococci in culture
(Griffon's technique)

CHAPTER THREE.

PATHOLOGY AND BACTERIOLOGY.

The clinical aspects have already been summarised and it is here proposed to deal with the pathological and bacteriological findings.

Histopathology.

Biopsies have been made and the histopathology studied in a number of cases by the author. The following description applies to a typical active ulcer as seen in Lagos.

The epidermal layer is greatly thickened in the region of the ulcer. Parakeratosis and a thickened horny layer are present. There is marked acanthosis, oedema of the rete Malpighii and formation of secondary papillae. The basal layer is several cells deep and shows numerous mitoses. At the edge of the ulcer the epithelium terminates abruptly.

There is marked oedema and congestion of the papillary region of the corium. Many of the vessels are replete with leucocytes and are surrounded by a plasma cell and

polymorph infiltration. The corium in proximity to the ulcer is diffusely infiltrated with polymorphs, lymphocytes and dense conglomerations of plasma cells. Many of the connective^{tissue} cells are laden with pigment. The ulcer itself is covered with an exudate composed of fibrin, blood and inflammatory cells. Just deep to the surface are numerous haemorrhagic areas. Next to this comes a layer of markedly congested blood vessels lying in an oedematous infiltrated tissue. More deeply are well developed blood vessels with dense zones of surrounding infiltration. Multinucleate cells are found, but rarely true giant cells. In the deeper parts the infiltration may extend down among the muscle fibres in dense columns composed of round and plasma cells. That marked vessel changes may occur in chronic cases is well illustrated by the accompanying microphotographs. In such an ulcer there must be serious interference with the blood supply and therefore great delay in healing.

Demonstration of the organisms in sections. Prolonged staining with Giemsa was found to display the organisms, particularly the fusiform bacilli, fairly well. Superficially there exists a mixture of organisms including paired cocci and cocci in chains and groups, spirochaetes and fusiform bacilli, the latter frequently appearing in bunches. In a deeper plane

a thick palisade -like mass of fusiform bacilli and scanty spirochaetes is frequently observed.

In many instances, including experimental ulcers, the fuso-spirochaetal symbiosis is found here and there to have almost replaced the normal capillary walls. The contents of the capillaries so affected are made up of fibrinous clots. It is possible that this may account for some of the tissue necrosis by cutting off the blood supply.

There has been some controversy as to whether the fusiform bacilli or the spirochaetes invade the tissue more deeply. Hallenberger(46) found that the bacilli advance into the tissues and prepare the way for the spirochaetes. Mayer(47) refers to Hallenberger's article and is surprised that this author describes the reverse to his own findings in collaboration with Keysselitz. They found the spirochaetes invaded the tissues deeply while the fusiform bacilli made a wall more superficially. Mayer was able to demonstrate the same arrangement in experimental amoebic ulceration of cats' intestines. The fuso-spirochaetal symbiosis is frequently found in the normal intestine of this animal and in the experimental ulceration the spirochaetes were seen in thick rows even amongst the septa of the inner muscle coat. Mense(48)

studying tropical ulcer, found the spirochaetes to precede the fusiform bacilli in the tissues. In sections stained by Warthin's method(49) the spirochaetes and fusiform bacilli show up well. The present writer, using this method, has been able to confirm Mense's observations, the spirochaetes being found in the deeper planes unaccompanied by fusiform bacilli. The spirochaetes alone were also seen in several instances to invade the rete Malpighii at the sides of the ulcer to a considerable depth. With the exception of the organisms the histopathology of *ulcus tropicum* does not present any specific features.

Autopsy.

Smith(6) in Lagos, records a post-mortem examination on a case of tropical ulcer . . The patient, who had a large ulcer on the left leg, died, in spite of various attempts at treatment, after being in hospital for over four months .

Post-mortem appearances.

It has been considered advisable to give these in detail as no other reference to findings at autopsy has been discovered in the literature available.

The patient was a male native aged eighteen years and the examination was performed within one hour of death.

General appearance. Marked emaciation.

Abdomen. No peritonitis or excess fluid,
generalised enlargement of the lymph glands.

Kidneys. Normal in size, opaque on section.

Liver. Large. Cut surface dull and
slightly granular. Negative for amyloid change.

Spleen. Small and firm.

Thorax.

Heart. Valves and aorta normal, muscle
tissue dark and soft.

Lungs. No adhesions, organs collapsed.
Small darkly mottled lymph glands in both groins.

Cultures. Aerobic cultures made on agar and
in broth from heart's blood, spleen, kidney, liver, glands
in groin and mesentery, were all negative.

Stained smears from the above organs revealed no
bacteria or spirochaetes.

Sections. These were made from all the organs , the
only findings worthy of record were in those stained
for fat by Sudan¹¹¹ :-

Liver. Diffuse fatty degeneration involving the whole lobule.

Kidney. Faint traces of fatty
degeneration.

It is concluded from these findings that the condition
was a toxæmic and not a septicæmic one.

Bacteriology.

Technique of routine examination.

The following procedure was carried out in each of the fifty clinical cases recorded in the appendix and it also formed the basis of bacteriological examination in a considerable number of other cases observed during the authors study of tropical ulcer in Lagos.

(A). Examination of the ulcers.

1. Dark-ground examination. This was employed mainly for the identification of the spirochaetes and certain "elongate organisms" to which further reference will be made.

2. Smears. These were taken and stained by the following methods :-

(a). Fontana. Technique as described in the second edition of Mackie and McCartney's "Introduction to Practical Bacteriology". A most useful stain for the morphological study of the spirochaetes and in estimating their relative number in proportion to the fusiform bacilli.

(b). Giemsa. Technique :- Fix smears in methyl alcohol - five per cent Giemsa in glass

distilled water for 24 hours with one change - decolourise with concentrated tannic acid solution - wash in distilled water, dry and examine. For permanent mounting the smears, after washing in distilled water, were carried rapidly through descending strengths of acetone in xylol and mounted in Canada Balsam. The Giemsa stain was found particularly useful for bringing out the finer details of morphology of the fusiform bacilli. Good differentiation is obtained with acetone.

(c) Carbol fuchsin. Used in strong solution this stain proved a rapid and fairly accurate method of gauging the relative number of spirochaetes and fusiform bacilli present.

(d) Gram's stain. Jensen's modification was employed with dilute carbol fuchsin as the counter-stain.

3. Agar cultures. These were made in order to ascertain the variety of organisms present which would grow under aerobic conditions at 37 c. on ordinary solid media.

(B). Examination of the buccal cavity.

This was carried out in the fifty clinical cases in order to ascertain if spirochaetes and fusiform bacilli of similar types to those found in the ulcers were harboured.

Technique. Material was obtained from the vicinity of the gums by means of a dressed probe and examined by the dark-ground. Smears were also made and stained by the methods of Fontana and Giemsa.

From the clinical case record it will be seen that in 86% spirochaetes were found and in 48% fusiform bacilli. In 44% there were spirochaetes of a similar type to those found in the ulcers ie. *Treponema schaudinni*. In one case there were fusiform bacilli only, and one other showed spirochaetes of the *T. schaudinni* type but no fusiform bacilli.

Burnie(10) in Northern Nigeria, found fusiform bacilli and spirochaetes, apparently identical with those of tropical ulcer, in the gums of 50 unselected hospital patients. He states that these organisms were also found in scrapings from the intact skin of non-ulcer cases.

It is worthy of mention that Vincent's angina as a clinical entity is not common in Lagos.

From the foregoing observations the mouth would appear

to be a possible source of the fuso-spirochaetal symbiosis of *Ulcus Tropicum*.

Organisms.

The flora in tropical ulcer is a very mixed one owing to external contamination and the use of native remedies. Various organisms have been incriminated and, in the course of my investigations, the following have been found in the lesions examined.

1. Spirochaetes of the type named *Spirochaeta schaudinni*. Prowazek. 1907. Or *Treponema schaudinni*.
2. Fusiform bacilli of a similar type to those found in Vincent's angina.
3. Elongate Gram-negative organisms.
4. Bacilli of the *Pseudomonas* group.
5. Diphtheroid bacilli.
6. Gram-positive cocci, including staphylococci and haemolytic streptococci.
7. Fungi of various types.

Spirochaetes and fusiform bacilli.

Spirochaetes and fusiform bacilli in combination have been observed in a number of situations in man but whether they are the same organism in every case remains to be proved. They have been found in the



mouth in normal individuals, in Ulcus Tropicum, ulcerative stomatitis, Vincent's angina and various other pathological conditions.

Tunncliffe(50) considers the fusiform bacilli and spirochaetes to be merely different forms in the life-cycle of one organism. Sanarelli(51) is of the same opinion and has named the common organism "Héliconème vincenti" . Pratt(52) and Gins(53) on the contrary , hold them to be entirely different organisms. Attempts at cultivation carried out recently in Lagos by Smith(54) and the present writer tend to support the latter view. Mixed cultures of fusiform bacilli showed no mutation into spirochaetes over a period of several months. It has already been mentioned under "Diagnosis" that examination of the secretion of tropical ulcers in Lagos invariably reveals the presence of spirochaetes and fusiform bacilli . It is only in cases which have reached the granulating stage or which have been under treatment for some time that these organisms are absent . Forty seven of the fifty clinical cases recorded in the appendix showed both organisms. In the remaining three fusiform bacilli alone were observed , two of the ulcers being at a late stage and one having received previous antiseptic treatment.

In the second edition of Kolle und Wassermann(55) it is noted that Vincent (1896) held spirochaetes and fusiform bacilli to be the cause of tropical ulcer. Keysellitz and Mayer (1909) are referred to as considering both parasites of significance in the aetiology . It has been thought advisable first to give a brief description of the spirochaetes and fusiform bacilli and then to mention some recent attempts at cultivation carried out in Lagos.

Spirochaetes.

Prowazek(56) has given a minute description of the spirochaetes of tropical ulcer which he named *Spirochaeta schaudinni*. The organism as observed by the present writer is, in general, from 10 to 20 u in length, about 0.5 u in breadth, actively motile and has a varying number of relatively shallow coils.

It stains pink with Giemsa and is decolourised by Gram. As seen by dark-ground illumination it is highly refractile , and a noteworthy feature in material taken direct from an ulcer is the great variation in length. Transverse division has been observed in mixed cultures . The organism is aerobic and facultatively anaerobic. In material from an ulcer mixed with a little broth the spirochaetes remained active for fourteen days at 10 degrees C.

Prowazek(56) and Mense(48) have described an undulating membrane and longitudinal division but Ford(57) points out that these findings lack confirmation. Prowazek also described sexual forms and resting stages. Pure cultures of the spirochaetes have not yet been obtained.

Fusiform bacilli.

The fusiform bacillus of tropical ulcer corresponds very closely to the type found in ulcerative lesions of the throat and first described fully by Vincent in 1896. The correct name appears to be *Fusiformis fusiformis* .

The organism as observed by the present writer presents the following characteristics:- The length is extremely variable , the typical bacillus being from 7 to 14 microns with a breadth of approximately 0.8 microns. It is thickest in the middle and tapers towards each end though occasionally club forms are seen . It may be straight or slightly curved . The shorter forms are often arranged in pairs end to end . In smears the organism may be remarkably pleomorphic. Three main types are observed . (1). A short broad type. (2). A short

slender type. (3). A long filamentous type up to thirty microns in length.

The bacillus stains irregularly. The reaction to Gram is variable, the majority being Gram-positive. Giemsa stain brings out marked beading. In a few instances globoid bodies, staining intensely with aniline dyes, were observed within the bacilli.

As a rule they were single but occasionally two were found in one organism. The majority were situated centrally though they were sometimes sub-terminal. In diameter the body was equal to or greater than that of the bacillus. These bodies were also seen in one instance during examination of fresh ulcer material under the dark-ground, conclusive evidence that they were not artefacts of staining. The foregoing description is illustrated by microphotographs. It is considered that bacilli showing such bodies may be involution forms. Ford(57) mentions similar "Coccus-like bodies" in cultures of *Fusiformis dentium*.

The majority of writers describe fusiform bacilli as non-motile though Topley and Wilson(58) note that some species may show motility. The present writer has observed sluggish motility in most of the specimens of ulcer material examined by the dark-

ground. Fusiform bacilli have been obtained in pure culture by various workers and will be alluded to later.

Elongate Gram-negative organism.

This organism, seen in a number of the ulcers in Lagos, presents characteristics intermediate between the spirochaetes and fusiform bacilli. In those ulcers in which it preponderated it was found to be associated with a markedly sanguineous discharge.

The organism was first alluded to by Smith(54).

It has the following characteristics:- the length is variable, from 7 to 28 microns , and the diameter is rather greater than that of the spirochaete.

It is motile but lacks the rapid spirochaetal movement and, when observed by the dark-ground, it appears to worm its way amongst the cellular debris of the ulcer exudate. In stained smears it is not possible to differentiate it with certainty from the spirochaete . Like the latter organism it is Gram-negative and this may help to distinguish it from the filamentous fusiform bacilli which are usually Gram-positive. When present in large numbers the organisms tend to be aggregated into bundles . It has been grown in mixed culture with the fusiform bacilli under anaerobic conditions, v. infra.

Cultivation of the spirochaetes and fusiform bacilli.

The spirochaetes.

The first successful attempt to cultivate the spirochaetes of tropical ulcer was made by Muhlens(59) who obtained a mixed culture on horse serum. The spirochaetes died out after three subcultures . Sanarelli(51) has cultivated apparently identical organisms from the guinea-pig in a medium containing *B. mesentericus vulgatus* or its filtered products. Fox(9) working on Naga sore, cultivated the spirochaetes anaerobically in one instance. Smith(54) in Lagos, first attempted to cultivate the spirochaetes on semi-solid serum, ascitic and hydrocele agar under anaerobic conditions but was not successful . Later, using a modified Wenyon's medium he was able to maintain the spirochaetes in culture over many generations. The present writer has recently obtained similar results in a number of cases by the same technique. The medium is made up as follows:- Forty ccs of 2% nutrient agar are added to 320 ccs of normal saline in a flask and autoclaved. Fifteen ccs of blood are obtained from a patient and added to the flask. The contents are then mixed by agitation and immediately distributed by sterile syphon into long

narrow test-tubes where a diffuse coagulum is formed. Retraction of the blood into a firm clot sometimes occurs but does not result in so good a medium.

Inoculation.

The superficial secretion is removed from an ulcer with swabs soaked in sterile water.

The exudate from the base is examined for spirochaetes by the dark-ground and then collected in a capillary pipette by means of which it is distributed into the upper third of the media in the culture tubes.

About 0.5 cc . of the exudate is added to each tube.

The tubes are incubated at 37 c. aerobically.

Examination.

At the end of four days the cultures are examined by the dark-ground and , if positive , numerous active spirochaetes as well as various contaminating organisms are seen . Smears are also made and stained by Fontana and carbol fuchsin.

Subculture.

The optimum time for subculture was found to be every five days. Some of the strains passed through sixteen subcultures before dying out.

The following observations can be made as a result of daily examination of these cultures . The spirochaetes are aerobic , growing best in the upper third of the media, and facultatively anaerobic in that they will grow when the tubes are sealed with a layer of liquid

paraffin. They tend to die out when the coagulum is destroyed by haemolysis, which is most probably brought about by the contaminating organisms.

Growth can be maintained at room temperature (27 to 30 c. in Lagos) but not at 10 C in a frigidaire.

The optimum temperature is 37 C. In most cases the spirochaetes die out by the end of twelve days if not subcultured though active forms have been noted up to three weeks in one or two of the cultures.

Multiplication by transverse fission was observed in the cultures by means of the dark-ground. The time taken for complete fission was about twenty minutes.

The spirochaetes increase greatly in length when cultured though numerous short forms are also present.

The fusiform bacilli.

According to Forde(57) pure cultures of fusiform bacilli were first obtained by Veillon and Zuber from the pus in a case of appendicitis. Later, Tunnicliffe(60) cultured them from cases of Vincent's angina. Fox(9) obtained pure cultures by the method of Krumwiede and Pratt. Kaspar(61) was able to cultivate the organism from liver and brain abscesses. All these writers found anaerobic conditions essential. In the present instance the bacilli were found to grow well under anaerobic conditions (Bullock's jar) in the

media used for the spirochaetes, and also in serum agar. No mutation into spirochaetes was observed. Recently, attempts have been made to isolate the organism in pure culture by the method of Krumwiede and Pratt(62) but so far have not been successful. Heavy contamination, mainly with streptococci and diphtheroid bacilli, is the chief obstacle.

The elongate Gram-negative organisms.

These organisms have been maintained in mixed culture with the fusiform bacilli in the modified Wenyon's media under anaerobic conditions for several months. No spirochaetes have been found in these cultures.

Pseudomonas pyocyanea.

This organism is present in nearly all of the ulcers seen in Lagos and undoubtedly plays a considerable rôle with reference to the duration of the lesion and the toxic effects. In morphology, staining reaction and biological characters it conforms to the descriptions given in the standard text-books on bacteriology. Pigment formation is variable though most strains produced a greenish blue pigment soluble in chloroform ie. pyocyanin, on agar slopes at room temperature. The organism was found to be most prevalent in the rainy season and it is noteworthy

that Burnie(10) did not find it common in tropical ulcer in the dry sandy locality of Kano in Northern Nigeria.

Pathogenicity.

Strains isolated in Lagos have been proved virulent for guinea-pigs and rabbits. Intraperitoneal inoculations using one cc of a twenty four hour broth culture caused death of the animals in one to two days with signs of acute peritonitis and septicaemia.

Subcutaneous inoculation with small doses gave rise to abscess formation which, in one or two instances, went on to a spreading ulceration . Two male patients were inoculated intracutaneously with 0.5 cc of an emulsion in sterile saline of a twenty four hour agar culture. In both cases a large boil-like lesion resulted which healed readily under simple measures. One of the patients had an initial sharp rise of temperature, in the other the temperature remained normal.

In several cases coming under the writer's observation an ulcer has almost healed only to break down again and spread rapidly. *Ps. pyocyanea* has been readily isolated from such cases . Examination has failed to reveal spirochaetes or fusiform bacilli nor does the ulcer take on its former phagedaenic character but tends to remain superficial and free from slough.

Diphtheroid bacilli.

These organisms have been isolated from a number of the ulcers and were found to be most prevalent in the dry season. They conform to the description of *Corynebacterium* as given in the Medical Research Council's "System of Bacteriology" (63). On nutrient agar at 37 C. in 24 hours the bacillus gives rise to small, round, opaque colonies 0.5 to 1.0 mm in diameter, dull white in colour, convex in shape and with an entire edge. In nutrient broth at 37 C. in 24 hours growth is fairly luxuriant and may occur at the surface in the form of a flaky pellicle or as a deposit at the bottom of the flask. Acid is produced in glucose and maltose in 24 hours. Some strains also ferment saccharose. The organisms have been isolated from anaerobic plates, while attempting to culture the fusiform bacilli, as well as from aerobic agar slopes during the routine examination of ulcers. One strain, isolated by the former method, failed to grow on nutrient agar under aerobic conditions but produced pin-point colonies on human blood agar slopes in 24 hours at 37 C. This strain when cultured on anaerobic serum agar plates showed extremely bizarre forms, some of the organisms presenting globoid swellings similar to those observed in the fusiform bacilli.

Pathogenicity.

Intradermal inoculation into guinea-pigs with 0,5 cc. of an emulsion in broth of a 24 hour blood agar culture produced in 48 hours a small boil from the pus of which the organisms were recovered in pure culture. Smears showed active phagocytosis. The lesions healed in five to seven days. A similar reaction was obtained in *Macacus rhesus* monkeys. Intraperitoneal inoculation of 0.5cc. of a 24 hour broth culture into guinea-pigs remained negative with all the strains used.

Four human volunteers , inoculated intradermally as in the guinea-pigs, showed in 48 hours a purulent vesicle about the size of a sixpence at the site of injection. From the pus the organisms were recovered in pure culture. The lesions healed in about seven days.

Toxin production.

Two strains , one isolated from an aerobic agar slope and one from an anaerobic serum agar plate , were tested for toxin production. In each case the organism was grown for nine days aerobically at 37 C. in fifty ccs. of broth in a wide flask. Both strains grew as a surface scum. At the termination of the incubation period the contents of the flasks were passed through fine grade

Seitz filters and tested for sterility.

A half cc. of the sterile filtrate was inoculated intradermally , first into guinea-pigs and afterwards into humans. The former showed no reaction. The latter presented , in 24 hours, a circumscribed erythematous area about the size of a penny at the site of inoculation. This disappeared in 72 hours. Controls were carried out in the same subjects using sterile broth and remained negative. These strains do not seem capable therefore, of giving rise to potent toxins.

Gram-positive cocci.

(a). Staphylococci,

Staphylococcus(*pyogenes*) *aureus* and *albus* are found in almost every case of tropical ulcer in Lagos and tend to persist when the other organisms have disappeared , thus no doubt helping to retard the process of healing.

(b). Streptococci.

These organisms are also extremely common . They have been isolated from the ulcers in serum broth by Griffon's technique and also from anaerobic serum agar plates in which they grow profusely. In smears from the ulcers diplococcal forms are common . On human blood agar plates they are seen to be markedly haemolytic. In morphology and cultural characteristics these cocci conform to the description of

Streptococcus pyogenes as given in the standard text-books on bacteriology.

Pathogenicity.

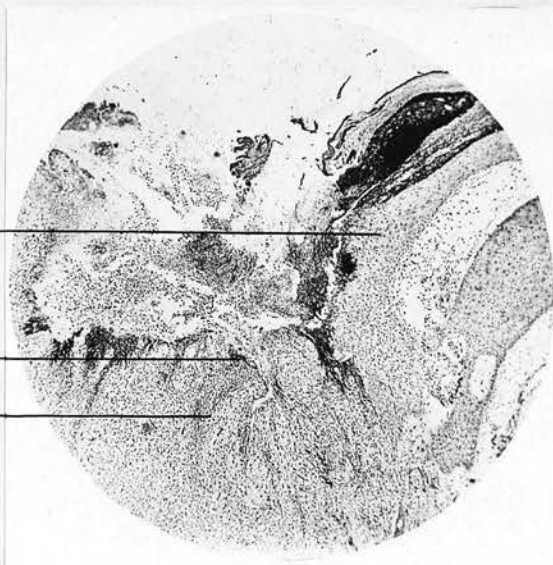
Subcutaneous injection with 0.5 cc. of an emulsion in sterile broth of a 24 hour blood agar slope causes a localised abscess in rabbits. Similar lesions were produced in human volunteers by intradermal inoculation.

Fungi.

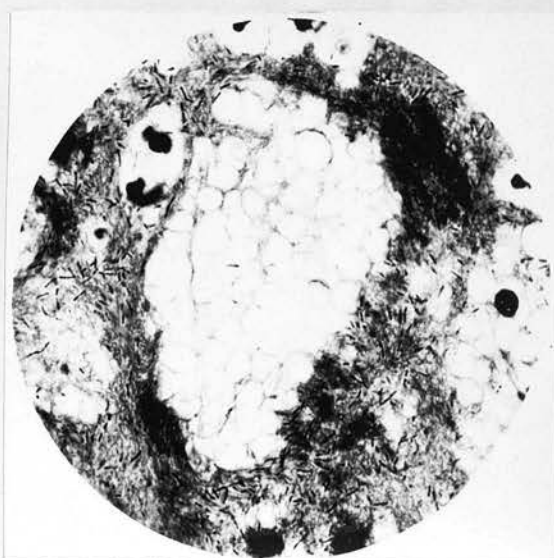
Various types of *aspergillus* and *penicillium* can be isolated from the ulcers but are not regarded as being endowed with pathogenic properties.

End of chapter three.

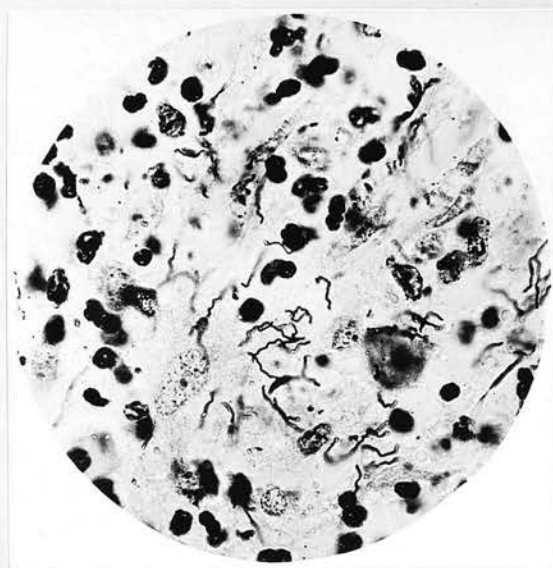
PATHOLOGY.



Low power view
of an ulcer.



1. Massing of fusiforms
around a capillary. x850



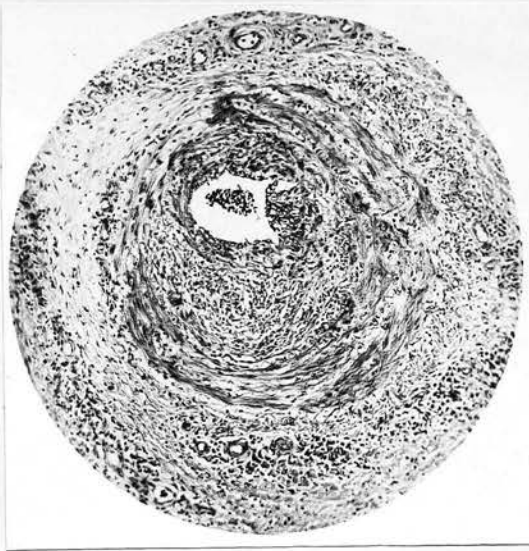
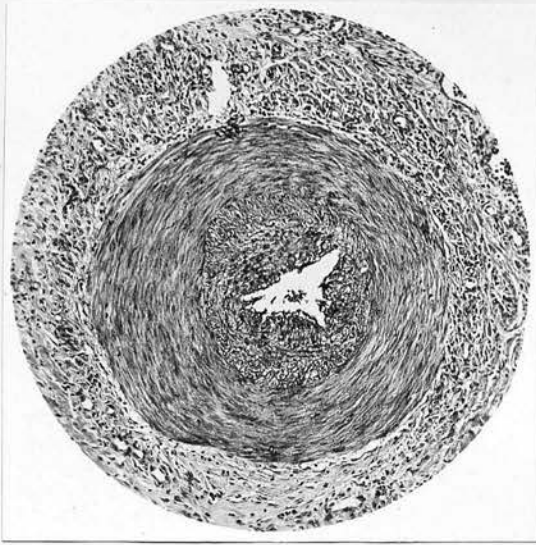
2. Spirochaetes
invading base. x850



3. Spirochaetes
invading epithelium. x850.

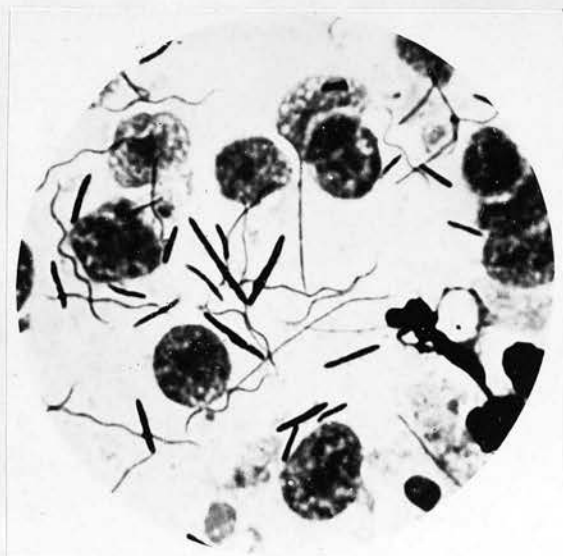
(Warthin stain)

PATHOLOGY.

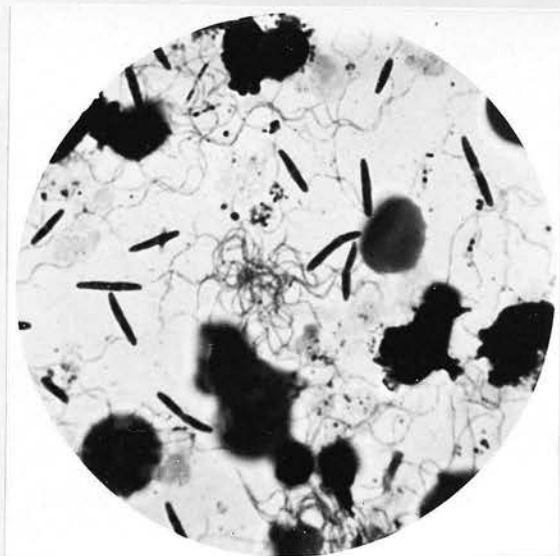


Marked vessel changes in the floor of a chronic tropical ulcer.

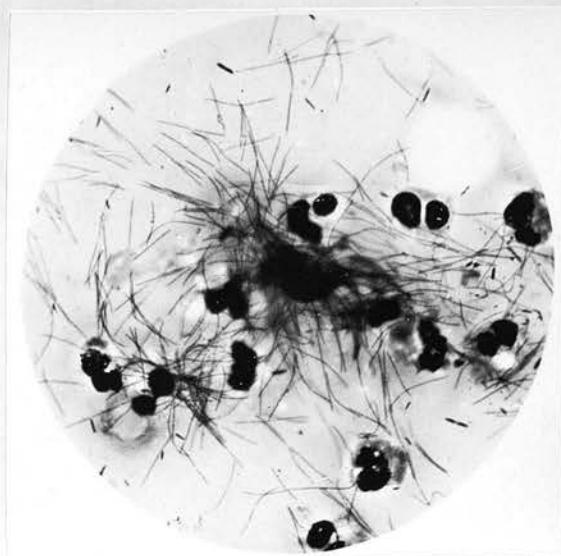
SMEARS FROM TROPICAL ULCER.



Spirochaetes and fusiform bacilli.



Spirochaetes
predominant.



Elongate organisms
predominant.

(Giemsa stain).

FUSIFORM BACILLI.

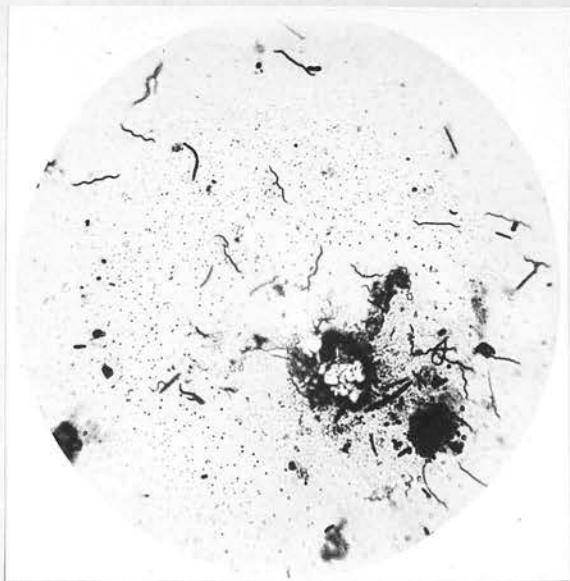


Illustrating filamentous forms and globoid bodies.

MOUTH SMEARS STAINED BY FONTANA.

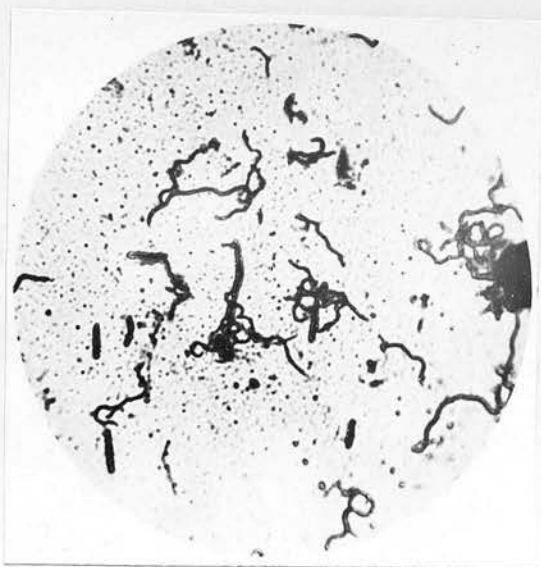


Ulcer case no. 42.



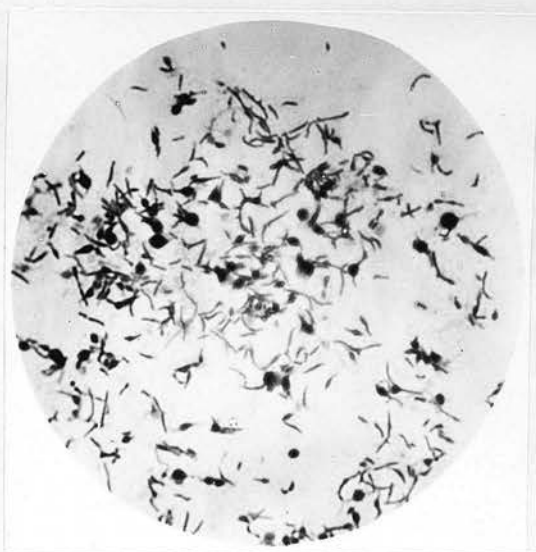
Ulcer case no. 35.

CULTURES IN MODIFIED WENYON MEDIUM.



Cultures at sixth passage stained by Fontana.

DIPHTheroid BACILLI.



Involution forms in anaerobic cultures.

CHAPTER FOUR.

EXPERIMENTAL.

Comparatively few experiments have been carried out in the production of tropical ulcer and the aetiological importance of the various organisms found remains obscure. In Kolle und Wassermann(55) it is noted that Vincent (1896) held the spirochaetes and fusiform bacilli to be the cause of tropical ulcer. Among later writers Keysselitz and Mayer (55) , Balfour(64) , Wolbach and Todd(22) , Adams(17) and Onorato(24) consider these organisms of aetiological importance and this is probably the general opinion at the present time.

Whether they can, by themselves, produce the ulcer or whether they require the help of other organisms such as the diphtheroid bacilli , pseudomonas, streptococci etc. remains to be proved. Certain factors of lowered resistance or vitamine deficiency may also be essential. The work of Smith(65) is of considerable interest.

He isolated in pure culture from Vincent's angina *Treponema microdentium*, a small fusiform bacillus, a vibrio and a haemolytic streptococcus.

None of these alone would produce the disease but a mixture of all four resulted in a typical fusospirochaetal abscess in the groin of mice and guinea-pigs. The present writer has recently had the opportunity of carrying out a considerable number of experiments in animals and humans in conjunction with Smith(66). It is deemed advisable to recapitulate these and to include some further work of the author's the results of which have been of a confirmatory nature. The experimental work carried out in Lagos though admittedly neither complete nor conclusive has brought to light certain points of interest in the aetiology of *Ulcus Tropicum*.

Animal experiments.

Various workers have attempted to produce ulceration in animals with material from tropical ulcers but, in the majority of cases, without success.

Blanchard(67) quotes le Dantec (in Cochin China) as having produced a typical phagedaenic ulcer in a single instance in a guinea-pig by inserting under the skin a splinter of bamboo soiled with earth.

Thomson and Robertson(68) refer to the work of Strong and Shattuck 1927, who obtained positive results in monkeys by inoculating ulcer material into previously devitalised skin.

In Lagos experiments were first carried out on *Macacus rhesus* monkeys, twenty animals being used in all. They were inoculated with material from typical ulcers on areas of skin previously devitalised with strong K.O.H. solution. Later, epilation of the site was found to answer the purpose as well as the K.O.H. The inoculum was obtained by first cleansing the surface of the ulcer with saline and then aspirating by capillary pipette the discharge from the base. Prior to inoculation the fluid was examined by dark-ground to confirm the presence of active spirochaetes and fusiform bacilli. The amount injected was a quarter to half a cc. Varying results were obtained in twelve of the animals, the remainder being entirely negative. In only one of the twelve was a well marked small ulcer seen. This commenced within two days of the inoculation and lasted four days, spirochaetes and fusiform bacilli being seen by dark-ground examination. A control area of devitalised skin was negative, remaining dry and unbroken. Transfer of the discharge to another

monkey was without result. In the remaining eleven monkeys abscess formation occurred in all at two to four days after inoculation, the control areas being negative. In the pus from the abscesses scanty spirochaetes and fusiform bacilli could be found up to the third day. After that time pseudomonas, streptococci and staphylococci dominated the picture. In two cases the abscesses persisted for eight days and the discharge contained numerous elongate Gram-negative organisms. A parallel series of inoculations was made into the testis, without previous preparation of the site, with negative results.

The results of experimental inoculation of ulcer material into *M. rhesus* monkeys are of little value, these animals being evidently unsuitable.

Similar experiments were later carried out on rabbits and guinea-pigs but the extreme susceptibility of these animals to pseudomonas infection rendered them even less suitable. Sheep, rats, and white mice were used with negative results. As a disease similar to tropical ulcer is said to occur in pigs experimental inoculation with ulcer material was carried out on two young animals both with and without previous devitalisation of the skin. No ulceration was produced. Intratracheal injection of ulcer material

in *M. rhesus* monkeys was made with negative results.

Human experiments.

The first successful attempt to produce tropical ulcer experimentally in man appears to have been made by Blanchard(67) who obtained a typical lesion by inoculating material from an ulcer into an area of skin previously devitalised by K.O.H. solution.

Balliano(69) produced experimental lesions in a series of twenty-six cases by autoinoculation with pus from tropical ulcers. In the report of the Pasteur Institute, Shillong(18) it is recorded that Hall Wright produced a Naga sore experimentally by feeding small flies of the *Siphonella* species on a lesion and then transferring them to a trivial abrasion on his own arm.

Fox(9) also working on Naga sore, succeeded in one instance in producing a typical ulceration by subcutaneous inoculation of the pus from a lesion. He mentions that, in this case, the fusiform bacilli appeared first, the spirochaetes later but finally predominating. Apostolides(19) in Palestine,

obtained typical ulcers in two cases by inoculating scarifications on the skin of healthy subjects with pieces of pseudo-membrane from Vincent's angina.

He considered this to be proof of the identical nature of the organisms in the two conditions.

Recently, Burnie(10) in Northern Nigeria, has produced experimental lesions in six cases.

Material from tropical ulcers was inoculated in one instance into an area of skin previously devitalised with pure carbolic, in three instances by inserting a small piece of ulcer tissue subcutaneously, and in two instances by applying the pus to naturally acquired trivial abrasions. In Lagos, owing to the difficulty of obtaining suitable subjects, it was thought advisable to use only one form of technique in order that results might be more easily comparable.

In all the experiments inoculation was made intracutaneously by means of a hypodermic syringe.

Twelve experimental inoculations were made in native volunteers, the inoculum consisted of an emulsion in sterile water of the superficial scrapings from typical ulcers after removal of the surface discharge.

The material was first examined by dark-ground to confirm the presence of active spirochaetes and fusiform bacilli. The amount injected was half a cc.

All the subjects were in good general condition and, being hospital patients, were living in hygienic surroundings on a liberal diet. In six of the cases results were obtained, the inoculation being

autogenous in three. The material used in one of the cases was obtained from an experimental ulcer at the eleventh day, the remaining five being inoculated from natural ulcers.

In all six cases typical ulcers developed at the site of inoculation in from four to seven days, remaining active and increasing in size for periods varying from ten to twenty-one days. During the period of activity microscopical examinations (dark-ground and smears) revealed the presence of spirochaetes and fusiform bacilli. The fusiform bacilli were found to predominate at first, later the spirochaetes.

It is to be noted that in all the experiments sterile dressings (saline, hot fomentations or dry dressings) were applied as soon as ulceration set in. This probably helped to limit the ultimate progress of the lesions. In two of the experiments the patients were undergoing treatment with neo-salvarsan but this did not prevent the production of typical experimental ulcers. These experiments show that ulceration, similar clinically and microscopically to natural tropical ulcer, can be produced in suitable subjects by the inoculation of material as described. The material may be either autogenous or heterogenous, the positive results obtained with the former

demonstrating absence of immunity .

Pseudomonas pyocyanea was recovered from five of the experimental lesions and, in order to gauge its importance in the production of the ulceration , the following further experiments were performed .

Two convalescent natives were inoculated intra-cutaneously with one cc. of an emulsion in broth of three agar slopes of different strains of *Ps. pyocyanea*.

In both cases the reaction was of the nature of a delayed abscess formation and no true ulceration occurred. The abscesses pointed about the seventh day and from the pus the organism was recovered in pure culture. The lesions healed in two weeks under simple treatment(hot boric fomentation).

More recently the writer has been able to confirm the above experimental work by producing typical ulceration in two cases by the same technique.

Experiments with cultures.

As it seemed probable that much time would elapse before there could be any hope of obtaining pure cultures of spirochaetes and fusiform bacilli it was decided to conduct some experiments with the cultures in their present state.

Two types of culture in the modified Wenyon's media were available:-

(a). Aerobic cultures containing numerous spirochaetes, scanty fusiform bacilli , *Ps. pyocyanea* and Gram-positive cocci.

(b). Anaerobic cultures containing numerous fusiform bacilli, elongate Gram-negative organisms, *Ps. pyocyanea* and Gram-positive cocci. The spirochaetes died out rapidly under strict anaerobic conditions (Bulloch's jar) , and repeated examinations failed to reveal their presence in the cultures.

Eight experimental inoculations were made in native hospital patients convalescent from various conditions including yaws ulceration, guinea-worm and tropical ulcer. In each case the patient received an intra-cutaneous injection in the deltoid region with half a cc. of the culture material. All received, in the opposite arm, an inoculation of half a cc. of a pure culture of *Ps. pyocyanea* in the same medium in order to exclude results from this organism alone. In five of the cases results were obtained. In three of these aerobic were used and in two anaerobic cultures. The control injection of *Ps. pyocyanea* was negative in three. In one it gave rise to a mild boil-like reaction and in the other to local induration only. In all five cases typical ulcers developed at the site of inoculation in from four to seven days,

remaining active and increasing in size for periods varying from two to nine days. Microscopic examinations (dark-ground and smears) were made daily and revealed the presence of numerous spirochaetes and fusiform bacilli in the first three experimental lesions and of fusiform bacilli and elongate organisms, but no spirochaetes, in the remaining two.

Ps. pyocyaneus was recovered from all. As in the previous experiments sterile dressings were applied on the appearance of ulceration.

These experiments show:-

1. That the spirochaetes in mixed culture are capable of active proliferation when injected into the skin. Whether they could per se produce a lesion remains unproven.

2. That the fusiform bacilli, in combination with the elongate organisms and *Ps. pyocyaneus*, produce a lesion in which all three show active proliferation.

The control inoculation of *Ps. pyocyanea* in the same patient produced only a very mild reaction so that the increased pathogenic effect must be ascribed to the fusiform bacilli and elongate organisms.

3. That there was no evidence of mutation of fusiform bacilli into spirochaetes. In the lesions produced with the anaerobic cultures fusiform bacilli

were present up to seven days from the time of inoculation. No spirochaetes were seen though a careful microscopic examination by the dark-ground was made daily.

Filtration experiments.

The following experiments were carried out in view of the possibility of a filtrable virus being incriminated in the cause of tropical ulcer.

A typical ulcer was scraped with a Volkmann's spoon and the material so obtained emulsified in sterile broth. The emulsion was examined by dark-ground and smears to confirm the presence of active spirochaetes and fusiform bacilli. Two native volunteers were then inoculated intradermally in the left deltoid region with half a cc. of the emulsion. The remainder of the material was immediately filtered through a fine Seitz filter and the filtrate tested for sterility aerobically and anaerobically. The following day half a cc. of the filtrate was inoculated intradermally in the right arms of the same subjects. In both cases a typical small ulcer developed in four days at the site of injection of the unfiltered emulsion. The lesions remained active for five or six days during which period spirochaetes and fusiform bacilli were present in

abundance. The inoculation with filtrate was completely negative in both cases.

These experiments tend to exclude the possibility of a filtrable virus as the responsible agent in tropical ulcer.

End of chapter four.

EXPERIMENTAL TROPICAL ULCER.



Ulcers produced by the inoculation of material as described in the text, page. 71.

EXPERIMENTAL TROPICAL ULCER.



Ulcer produced with an aerobic culture.



Ulcer produced with anaerobic culture. (See page 74).

SUMMARY AND CONCLUSIONS.

Tropical ulcer has been described in its clinical aspects. Complications are referred to and the outstanding points in differential diagnosis noted. Such questions as geographical distribution, seasonal incidence, epidemiology, race, sex, age, have all found a place.

Immunity is regarded as being practically non-existent and this statement seems to be borne out by experimental work. Nevertheless, a certain degree of local immunity must develop as otherwise it would be difficult to understand why so many ulcers advance rapidly to a certain size and then suddenly slow down. It may be that there is a loss of initial virulence on the part of the infecting agent which is rendered less pathogenic by the host's protective mechanism.

The natural transmission of the disease has been alluded to. This is an aspect of first importance and well deserves the attention of entomologists and health workers in tropical countries. The fact that

an identical lesion, Naga sore, has been passively transmitted by a species of fly (Siphonella) as demonstrated by Hall Wright is significant but needs further elucidation as it does not bring one much nearer to a solution of what is the essential factor in the causation of tropical ulcer. In such mechanical transmission the complete and usually mixed flora may be carried over as opposed to the selective action of a developmental cycle within the insect. The same fallacy applies to such examples of direct inoculation as quoted by Cross, Peters, and Apostolides. It seems justifiable to conclude that a break in continuity of skin surface is essential to the production of a tropical ulcer, to venture further than this appears hazardous.

Under predisposing causes are mentioned trauma, climate, debility, dietetic deficiency. Dietetic deficiency with or without some added condition of debility may be the determining factor in the causation of tropical ulcer whereby the patient's resistance is lowered and the specific organism enabled to invade the tissues. This must remain only a supposition pending further work on these important questions.

It is obvious from a perusal of chapter two that there is no sovereign remedy for tropical ulcer.

Some measure of success will be obtained in certain cases with probably any form of treatment adopted and some will heal of their own accord without medicinal aid. Local neo-salvarsan seems to stand out as being successful in a fair percentage of cases and this is all the more striking when one considers the complete lack of response to the intravenous administration of the drug. Possibly the occlusion of the capillaries by the fusiform bacilli and the accompanying coagulation necrosis which is entailed thereby may act as a protective barrier for the organisms.

Owing to the fact that both the actual cause and the natural transmission of the disease are as yet vague, prophylaxis on a widespread basis is difficult if not impossible.

In the section devoted to pathology the author is forced, in common with other writers, to the conclusion that the only distinctive feature in the histopathology of tropical ulcer is the fusospirochaetal symbiosis. It is interesting to note the apparently greater invasive power of the spirochaetes for both connective and epithelial tissues. The post-mortem account fails to reveal any generalisation of either the fusiform bacilli or the spirochaetes.

Under Bacteriology the importance of dark-ground examination is stressed. Mouth findings are commented upon and a fairly⁺ comprehensive survey of the organisms found in tropical ulcer has been made. The successful cultivation of the spirochaetes would seem to bring us one step nearer the solution of the aetiological problem. It is hoped that, in course of time, pure cultures may be available for further work.

The role played by *Pseudomonas pyocyanea* is alluded to and the findings in connection with diphtheroid bacilli are treated fully. In connection with the later^t organisms, their toxin producing capacity was investigated and found to be negligible.

From a perusal of the animal experiments performed with ulcer material it becomes apparent that whatever the aetiological factor may be its host specificity is highly developed as in no animal was a successful result obtained. One is confined, therefore, to the use of human material — necessarily limited.

The human experiments demonstrate beyond all doubt:-

1. That ulcer material is infective for humans both autogenously and heterogenously.

2. That the spirochaetes and fusiform bacilli are transmissible and will proliferate given suitable

conditions.

3. That this form of ulceration can be transmitted in series from man to man. Increase of virulence by such passage was not noted.

4. That the inoculation experiments made with cultures demonstrate that typical ulceration is not obtained in the absence of the spirochaetes and fusiform bacilli.

5. That no evidence of mutation was found.

Since negative results were obtained in those inoculations made with filtered material the possibility of a filtrable virus being the aetiological factor would appear to be excluded.

Acknowledgments.

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A P P E N D I X .

CLINICAL CASE RECORD.

The fifty cases recorded in this appendix have been alluded to in various places in the text.

In the section on Bacteriology the technique of routine examination, as applied to each of these cases, has been described in full.

Under the heading "Patient" the tribe, sex, age and occupation are given in that order.

The following abbreviations have been employed:-

O.P. = Out-patient.

I.P. = In-patient.

D.G. = Dark-ground examination.

Spiros. = Spirochaetes.

Fus. Bac. = Fusiform bacilli.

Elongates. = Elongate Gram-negative organisms.

H . B. F.= Hot boric fomentation.

Patient.	History.	Clinical appearance.	D.G.	Smears.
(1). Yoruba. M. 21 years. Labourer. O.P.	Commenced at site of guinea-worm bleb six months ago.	Oval ulcer 3"diam, immed above L. medial malleolus. Regular raised edge, not undermined. Base of septic granulations covered with thick foul blood-stained discharge. Not very painful.	Spiros. + Fus bac.++	Spiros. ++ Fus bac.+++
(2). Warri. M. 20 years. Nil. O.P.	Commenced 3 weeks ago as small irritating bleb which he scratched and opened.	Two small rounded ulcers 1½" diam. One on ant.aspect lower third of R. leg, the other medial aspect lower third of L.leg. Regular edges, not thickened or undermined. Necrotic base covered with thick purulent blood-stained discharge. Foul smelling, Painful.	Spiros. ++ Fus bac. +	Spiros. ++ Fus bac. ++
(3). Ibo. M. 20 years. Carpenter. O.P.	Commenced 7 months ago at site of injury with a piece of metal.	Large oval ulcer 5x3" immed above L. lateral malleolus. Edges slightly raised and thickened, rather irregular. not undermined. Base of unhealthy granulations covered with sero-purulent discharge. Ulcer deepest at centre where it involved the periosteum. No marked odour. Not very painful.	Spiros + scanty. Fus bac. ++ Elongated + scanty.	Spiros + scanty. Fus bac. ++ showing marked beading.
(4). Yoruba. F. 15 years. Domestic servant. I.P.	Commenced one month ago at site of injury with a pointed stick. Treated with a native medicine of powdered leaves.	Oval ulcer 2x1", dorsum of R. foot. Edges regular, rolled appearance, not undermined. Raw bleeding base covered with thick grey discharge. Surrounding skin oedematous. Foul smelling. Painful. Slight ulceration 2nd and 4th toes of R. foot.	Spiros. ++ Fus bac. ++	Spiros. +++ Fus bac. ++
(5). Yoruba. M. 19 years. Labourer. O.P.	Commenced one month ago at site of abrasion.	Rounded ulcer 1½" diam, dorsum of R. foot at root of big toe. Edges slightly irregular and undermined. Base of unhealthy granulations covered with blood-stained purulent discharge. Ulcer somewhat superficial. Foul smelling. Not painful.	Spiros. ++ Fus bac. +	Spiros. ++ Fus bac. +
(6). Yoruba. F. 12 years. School girl O.P.	Commenced 2 months ago at site of abrasion.	Rounded ulcer 2"diam, lateral aspect upper third of R. leg. Edges slightly raised and indurated, not undermined, regular. Base of adherent yellow slough covered with thick greyish yellow discharge. Foul smelling. Somewhat painful. Surrounding skin oedematous.	Spiros. + Fus bac. +	Spiros. + Fus bac + many long forms.

Agar Culture.	Mouth.	Treatment.	Remarks.	Sheet (I).
(1) Gram + sporing bacillus. (2) Ps. pyocyanea.	Nil.	(1) H.B.F. (2) Picric lotion 1%.	General condition good. Attended for treatment a few days only. Ulcer much cleaner when last seen.	
(1) Ps. pyocyanea. (2) Gram + cocci.	Spiros+, a few of ulcer type. Fus bac + scanty.	(1) H.B.F. until cleaner. (2) Picric lotion 1%.	General condition good. At 8 days very little improvement. Did not attend for further treatment. Attempt to cultivate mouth spiro on mod Wenyon's medium and serum-agar failed.	
(1) Ps. pyocyanea. (2) Gram + cocci.	Nil.	(1) H.B.F. (2) Picric lotion 1%.	General condition good. Refused admission to hospital. Ulcer healed very slowly under ambulatory treatment. At two months half original size, septic granulations. No spiro or fus bac seen by D.G. and smears.	
(1) Ps. pyocyanea. (2) Gram + cocci. (3) Gram + sporing bacillus.	Spiros+, a few of ulcer type. Fus bac + scanty.	(1) H.B.F. (2) Eusol bath followed by picric dressing. (3) Injections of neo-salvarsan, total 3.3 grams.	General condition poor. Ulcer rapidly improved under local treatment. Neo-salvarsan commenced 6 days after admission. Ulcer completely healed in 4 weeks.	
Ps. pyocyanea.	Spiros+, very scanty, none of ulcer type. Fus bac + ?	(1) H.B.F. (2) Picric lotion 1%.	General condition fair. Characteristic discharge cleared up in 4 or 5 days. At 7th day no spiro or fus bac seen by D.G. and smears. Healed very slowly-- 2 months.	
(1) Ps. pyocyanea. (2) Gram + cocci.	Spiros+, none of ulcer type. Fus bac. +	(1) H.B.F.	General condition poor. Very little improvement in 4 days with H.B.F. Refused admission to hospital and did not attend for further treatment.	

Patient.	History.	Clinical appearance.	D.G.	Smears.
(7) Yoruba. M. 13 years. School boy O.P.	Commenced one month ago at site of local injury.	Oval ulcer $1\frac{1}{2} \times \frac{1}{4}$ " over lower third of R. tibia. Edges regular, slightly thickened, not undermined. Base of adherent greyish-yellow slough covered with thick blood-stained discharge. Ulcer has a deep rather punched out appearance. Periosteum involved. Foul smelling. Very painful.	Spiros. +. Fus bac. +. Elongates. ++.	Spiros. ++. Fus bac. ++, mainly short forms.
(8) Hausa. M. 18 years. Nil. I.P.	Commenced 3 months ago at site of injury by a piece of wood.	Circular ulcer 3"diam. L. ankle anterior to lateral malleolus. Edges regular, slightly raised and thickened, not undermined. Base of greyish-yellow necrotic tissue covered with a thick sero-purulent discharge. Foul smelling. Painful.	Spiros ++. Fus bac ++.	Spiros ++. Fus bac ++.
(9) Zabaruma. M. 20 years. Nil. I.P.	Duration some months. Commenced at site of injury to old scar.	Oval ulcer 4X3" just above L. lateral malleolus. Edges raised, indurated, slightly undermined, regular. Base of tenacious greenish-yellow slough covered with a thick greenish discharge. Surrounding skin hyper-pigmented. Not very painful. Foul smelling.	Spiros +. Fus bac +. Elongates ++.	Spiros ++ Fus bac +, relatively scanty.
(10) Yoruba. M. 23 years. Labourer. I.P.	Patient states it commenced 3 weeks ago as a boil. No history of local injury.	Oval ulcer $2\frac{1}{2} \times 1\frac{1}{2}$ " over R. medial malleolus. Edges regular, oedematous, not undermined. Base of uneven yellow slough covered with a thick purulent discharge. Foul smelling. Not very painful. Marked oedema of surrounding skin.	Spiros ++. Fus bac ++.	Spiros ++. Fus bac ++.
(11) Yoruba. M. 22 years. Carrier. O.P.	Commenced 2 weeks ago at site of injury by a stone.	Small circular ulcer $\frac{3}{4}$ "diam, over lower third of R. tibia. Edges regular, not undermined. Base of greenish-yellow slough covered with thick blood stained discharge. Very foul smelling. Surrounding skin oedematous. Painful.	Spiros ++. Fus bac +. Elongates ++.	Spiros ++. Fus bac +.

Agar culture.	Mouth.	Treatment.	Remarks.	Sheet (2).
Gram + cocci.	Spiros+scanty, none of ulcer type. Fus bac +. scanty.	(1) H.B.F. (2) Picric lotion 1%. (3) Boric powder.	General condition fair. At 14 days ulcer granulating, no odour, sero-purulent discharge. No spiro, fus bac or elongate organisms seen by D.G. and smears. Ulcer healed in six weeks.	
Ps. pyocyanea. Gram+cocci.	Spiros+, a few of ulcer type. Fus bac.+.	(1) Six injections of neo-salvarsan, total 3.3 grams. (2) H.B.F. (3) Picric lotion 1%. (4) Pot permang lotion. (5) Alum acetate lotion. (6) Surgical measures ulcer scraped and edges pared. Thereafter dry dress- ings of boric powder.	Patient emaciated. No improvement in 6 weeks with local antiseptics and injections of neo- salvarsan. After scraping etc the raw surface remained clean and was soon covered with healthy granulations. Healed in about five weeks.	
Ps. pyocyanea. typical blue green pigment. Gram + cocci.	Spiros+, none of ulcer type. No fus bac seen.	(1) Ulcer scraped and edges pared. (2) Dry dressings. (3) Lotio rubra.	General condition very poor. Complained of starvation. After scraping, the raw surface remained clean. Healing was slow. Almost completely healed at end of three months.	
Gram + cocci.	Spiros+ scanty, none of ulcer type. No fus bac seen.	(1) H.B.F. (2) Picric lotion 1%. (3) Neo-salvarsan inject- ions, total 3.3 grms.	General condition good. Cleared up slowly, spiro and fus bac persisting in discharge for about 14 days. Healed at end of 2½ months.	
Ps. pyocyanea. Gram + cocci.	Spiros++, some of ulcer type. Fus bac+scanty.	(1) H.B.F. (2) Picric lotion 1%.	General condition poor. Ulcer cleared up fairly rapidly and was completely healed in 4 weeks. Elongate organisms not distinguishable from spirochaetes in stained smears.	

Patient.	History.	Clinical appearance.	D.G.	Smears.	Agar culture.
(12) Zabaruma. M. 18 years. Labourer. O.P.	Commenced one month ago at site of injury by a piece of iron.	Circular ulcer 4" diam immed above L. medial malleolus. Edges regular, slightly raised and thickened, not undermined. Base of ragged grey slough covered with a thick purulent discharge. Surrounding skin slightly oedematous. Not very painful.	Spiros++. Fus bac+.	Spiros++. Fus bac++.	Ps. pyocyanea. Gram + cocci. Diphtheroids.
(13) Yoruba. F. 8 years. Nil. O.P.	Commenced 2 months ago at site of minor injury.	Oval ulcer 1½x1" on post aspect of L. ankle. Edges regular, slightly raised and thickened, not undermined. Small bud-like extension at one place. Base of ragged greyish-yellow slough covered with thick blood-stained discharge. Foul smell. Very painful. Oedema of surrounding skin.	Spiros+. Fus bac++.	Spiros+. Fus bac++. numerous filamentous forms	Gram + cocci.
(14) Hausa. M. 24 years. Labourer. O.P.	Commenced 2 weeks ago as a small boil.	Circular ulcer 1½" diam. Ant aspect mid third of L. leg. Edges regular oedematous, not undermined. Base of slough covered with thick greyish discharge. Foul smell. Painful.	Spiros+. Fus bac+.	Spiros+. Fus bac+.	Ps. pyocyanea. Gram + cocci.
(15) Yoruba. M. 5 years. Nil. I.P.	Commenced 3 months ago at site of local injury.	Oval ulcer 2½x2" over R. lateral malleolus. Edges regular, slightly raised and thickened. Base of septic granulations covered with a thick greyish-green discharge. Surrounding skin oedematous and hyperpigmented. Foul smell. Painful.	Spiros++. Fus bac+.	Spiros++. Fus bac+, mainly short forms.	Ps. pyocyanea. Gram + cocci.
(16) Yoruba. M. 13 years. Nil. O.P.	Commenced 12 days ago at site of injury by a stone.	Circular ulcer 3" diam over lower third of R. tibia. Edges regular, swollen, not undermined. Base of tenacious slough covered with thick blood-stained discharge. Surrounding skin oedematous. Foul smell. Not very painful.	Spiros++. Fus bac++.	Spiros++. Fus bac++. very pleomorphic.	Diphtheroid bac. Gram + cocci.

Mouth.	Treatment.	Remarks.	Sheet 3.
Spiros+++ , many of ulcer type. Fus bac.+.	1. Ulcer scraped and edges pared. 2. Dry dressings. 3. Lotio rubra.	General condition poor. Marked pyorrhoea alveolaris. After scraping the raw surface remained clean. Healed slowly, in about 3 months.	
Spiros++ , some of ulcer type. Fus bac+.	1. H.B.F. 2. Picric lotion 1%.	General condition good. Mouth shows pyorrhoea. Patient attended for 4 weeks. Ulcer much cleaner when last seen, granulating. No spiro or fus bac seen by D.G. or smears.	
Spiros+ , none of ulcer type. No fus bac seen.	1. H.B.F. 2. Picric lotion 1%.	General condition poor. Ulcer healed slowly under treatment. Small area of weak granulations at end of six weeks.	
Spiros+ , a few of ulcer type. Fus bac.+.	1. Ulcer scraped and edges pared. 2. Dry dressings. 3. Lotio rubra.	General condition fair. After scraping the raw surface remained clean and the subsequent granulations were healthy. Completely healed in about 8 weeks.	
Spiros++ , none of ulcer type. No fus bac seen.	H.B.F.	General condition poor. Patient looks toxic. Refused admission and only attended O.P. Dept for three or four days.	

Patient.	History.	Clinical appearance.	D.G.	Smears.
(17) Yoruba. F. 2½ years. Nil. I.P.	Commenced 3 months ago as a small spot which became abraded.	Oval ulcer 4x3" post surface lower third of R.leg. Edges rather irregular, slightly thickened, not undermined. Large flap of skin separated from underlying tissue at one side and sloughing off. Base of ulcer underneath flap consists of necrotic slough, remainder of base composed of septic granulations. Thick greyish-yellow discharge. Surrounding tissues oedematous. Foul smell. Painful.	Spiros +. Fus bac++.	Spiros+, relatively few in number. Fus bac+++ ^{mainly} , mainly showing globoid bodies.
(18) Yoruba. F. 14 years. Hawker. O.P.	Commenced 6 weeks ago at site of minor injury.	Oval ulcer 1½x1" immed above L. medial malleolus. Edges regular, slightly raised and thickened, not undermined. Base of septic granulations covered with a thick greenish-yellow discharge, blood-stained. Foul smell. Painful.	No spiro seen. Fus bac++.	No spiro seen. Fus bac++ ^{mainly} , mainly short forms.
(19) Ijaw. F. 9 years. Nil. O.P.	Commenced one week at site of minor injury.	Circular ulcer 1" diam dorsum of R.foot. Edges regular, flat, not undermined. Base of septic granulations covered with thick tenacious discharge. Foul smell. Not very painful. Slight oedema of surrounding skin.	Spiros +. Fus bac++.	Spiros +. Fus bac+++ ^{mainly} mainly short forms. A few show globoid bodies.
(20) Ibo. M. 29 years. Labourer. O.P.	Commenced several months ago as result of injury by a piece of wood.	Circular ulcer 1" diam dorsum of R.1st toe. Edges regular, slightly raised and thickened, not undermined. Base of septic granulations covered with a yellow purulent discharge. Foul smell. Very little pain. Toe swollen and indurated.	Spiros +. Fus bac++.	Spiros +. Fus bac++.
(21) Yoruba. M. 10 years. School boy. O.P.	Commenced one month ago at site of injury by a pointed stick.	Oval ulcer 2½x1½" over lower third of L.tibia. Edges rather irregular, swollen, not undermined. Base composed of adherent slough covered with a thick greyish-yellow discharge. Foul smell. Painful. Oedema of surrounding skin.	No spiro seen. Fus bac++. Elongates†	No spiro seen. Fus bac++ ^{many} , many filamentous forms, some with globoid bodies. Elongates arranged in masses.

Agar culture.	Mouth.	Treatment.	Remarks.	Sheet 4.
Diphtheroid bac. Gram + cocci.	Spiros+, scanty, none of ulcer type. No fus bac seen.	Sloughing skin removed. 1. Warm cyllin baths twice daily followed by picric lotion 1%. 2. Neo-salvarsan I.M. injections.	General condition very poor. Child emaciated and fretful. Ulcer commenced to clear up fairly rapidly under treatment. At 14 days base was com- posed of healthy granulations except at lower edge where thick discharge contain- ing numerous spiros and fus bac persisted. At 21 days ulcer beginning to extend at lower edge, so patient anaesthetised and active area scraped. Thereafter healing was uninterrupted, the base remaining clean. Patient began to put on weight. Given Ol. morrhuae and extra milk in addition to ordinary diet. Ulcer completely healed in three months.	
Ps. pyocyanea. Gram + cocci.	Spiros+, scanty, none of ulcer type. No fus bac seen.	1. H.B.F. 2. Picric lotion 1%.	General condition good. At 5th day ulcer somewhat improved, discharge less copious and thinner. At 10th day sero-purulent discharge slight in amount. No fus bac or spiros seen by D.G. and smears. At 21 days ulcer almost healed.	
Ps. Pyocyanea. Gram + cocci.	Spiros+, very few. No fus bac seen.	1. H.B.F. 2. Picric lotion 1%.	General condition poor. Mouth healthy. Ulcer presented a clean granulating surface in 6 days. Healed in four weeks.	
Ps. pyocyanea. Diphtheroid bac.	Spiros+++ , many of ulcer type. Fus bac+.	1. H.B.F. 2. Picric lotion 1%. 3. Lotio rubra.	General condition fair. Mouth shows pyorrhoea. Healed very slowly. Small area of weak granulations at end of 6 weeks; scanty sero-purulent discharge showing no spiros or fus bac. Agar culture gave profuse growth of Ps. pyocyanea.	
Ps. pyocyanea. Diphtheroid bac. Gram + cocci.	Spiros+ , none of ulcer type. No fus bac seen.	1. H.B.F. 2. Picric lotion 1%.	General condition fair. Thick discharge cleared up in 10 days and slough separated. Healed in about 8 weeks.	

Patient.	History.	Clinical appearance.	D.G.	Smears.
(22) Yoruba. F. 24 years. Hawker. I.P.	Commenced 4 months ago as an itchy spot.	Circular ulcer 4" diam, medial aspect lower third of R.leg. Edges regular, slightly raised and indurated. Base of septic granulations covered with thick discharge. Foul smelling. Not very painful.	Spiros +. Fus bac++.	Spiros +. Fus bac++.
(23) Hausa. M. 25 years. Casual labourer. O.P.	Commenced 3 weeks ago at site of minor injury.	Oval ulcer 2½x1½ medial aspect of R. foot just below malleolus. Edges rather irregular, swollen, not undermined. Base of septic granulations covered with a thick blood-stained discharge. Foul smell. Not very painful. Surrounding skin oedematous.	Spiros++. Fus bac++. Elongates+.	Spiros++. Fus bac++. marked beading, some with globoid swellings.
(24) Yoruba. M. 8 years. School boy. O.P.	Commenced 3 weeks ago at site of abrasion by a piece of iron.	Oval ulcer 2x1" over lower third of R.tibia. Edges regular, rolled not undermined. Base of adherent greenish-yellow slough covered with a thick greenish blood-stained discharge. Foul smell. Painful.	Spiros +. Fus bac+.	Spiros + Fus bac++. mainly short forms.
(25) Yoruba. M. 6 years. Nil. O.P.	Commenced some weeks ago as an itchy spot.	Kidney shaped ulcer 2½x1½" on post aspect of L.ankle. Edges slightly raised and thickened, not undermined. Base of septic granulations covered with a thin purulent discharge. Painful. Not offensive.	Spiros +, scanty. Fus bac+, scanty.	Spiros +, scanty. Fus bac+, scanty.
(26) Yoruba. M. 30 years. Nil. I.P.	Commenced 2 weeks ago as an itchy spot.	Oval ulcer 4x3" lateral aspect lower third of L.leg. Edges regular, flat, not undermined. Base of necrotic sloughing tissue, very uneven. Thick blood-stained discharge. Surrounding tissues oedematous. Foul smell. Painful. A typical phagedaemic ulceration.	Spiros+++. Fus bac++.	Spiros+++. Fus bac mainly+++ short forms..

Agar culture.	Mouth.	Treatment.	Remarks.	Sheet 5.
Gram + cocci.	Spiros+, none of ulcer type. No fus bac seen.	1. H.B.F. 2. Cyllin baths. 3. Course of sulpharsenol.	General condition good. Ulcer very refractory to treatment. At 4 weeks ulcer cleaner and discharge less. Spiros and fus bac still present. At 6 weeks commencing to heal. Patient discharged for creating disturbance and advised attend O.P.Dept. At 10 weeks healing slowly, scanty sero-purulent discharge. No spiros or fus bac seen.	
Diphtheroid bac. Gram + cocci	No spiros or fus bac seen by D.G. and smears.	1. H.B.F. 2. Cyllin baths. 3. Picric lotion 1%. 4. Lotio rubra.	General condition poor. Ill nourished. Previous treatment with native medicine i.e. decoction of 'samiah' leaves taken internally, residue used as local dressing. Ulcer cleared up fairly rapidly but still presented an area of granulations the size of a florin at the end of 10 weeks.	
Ps. pyocyanea. Gram + cocci.	Spiros+++ , many of ulcer type. Fus bac+.	1. H.B.F. 2. Picric lotion 1%.	General condition fair. Mouth shows pyorrhoea. Slough separated in 5 days and there was much less discharge. Healed in about 6 weeks.	
Ps. pyocyanea. Gram + cocci.	Spiros++, none of ulcer type. No fus bac seen.	1. H.B.F. 2. Picric lotion 1%.	General condition good. Ulcer beginning to heal when first seen. Healed completely in 4 weeks.	
Ps. pyocyanea. Diphtheroid bac. Gram + cocci.	Spiros+, none of ulcer type. No fus bac seen.	1. H.B.F. 2. Cyllin baths. 3. Iodoform. 4. Neo-salvarsan injections total 3.3 grms.	General condition poor. Ill nourished. Ulcer rapidly improved with rest in bed, fomentations and cyllin baths. At 7 days much cleaner and commencing to granulate. First injection of neo-salvarsan. At 10 days discharge small in amount, no spiros or fus bac seen. At 6 weeks small healthy granulating area. Patient discharged to O.P.Dept.	

Patient.	History.	Clinical appearance.	D.G.	Smears.
(27) Zabaruma. M. 20 years. Labourer. I.P.	Commenced one week. No history of injury.	Circular ulcer 2"diam, lateral aspect upper third of R.leg. Edges swollen and necrotic. Base of sloughing tissue covered with a thick blood-stained discharge. Surrounding tissues oedematous. Foul smell. Remarkably little pain. A typical phagedaenic ulceration.	Spiros.+++. Fus bac +. Elongates+.	Spiros+++. Fus bac++, a few show globoid bodies.
(28) Jekri. M. 25 years. Nil. O.P.	Commenced two months ago at site of injury with pointed stick.	Circular ulcer 1½"diam just anterior to L. lateral malleolus. Edges regular, slightly raised, indurated, not undermined. Base of ragged slough covered with a thick yellowish blood-stained discharge. Hyperpigmentation of surrounding skin. Foul smell. Not very painful.	Spiros ++. Fus bac +.	Spiros +. Fus bac++, mainly short forms.
(29) Yoruba. M. 19 years. Labourer. I.P.	Commenced one week ago at site of injury with broken glass.	Oval ulcer 2½x1½" just above R. lateral malleolus. Edges flat, regular, necrotic. Base of ragged slough involving muscles. Thin blood-stained discharge. Surrounding tissues oedematous. Very offensive smell. Painful. A typical phagedaenic ulceration.	Spiros ++. Fus bac ++. Elongates+.	Spiros ++. Fus bac ++. Elongates.+.
(30) Zabaruma. M. 18 years. Nil. I.P.	Commenced several months ago at site of minor injury by a piece of wood.	Circular ulcer 1½"diam just above L.lateral malleolus. Edges regular, slightly raised and thickened, not undermined. Base of septic granulations covered with a thick yellowish blood-stained discharge. Foul smell. Not very painful.	Spiros ++. Fus bac +.	Spiros ++. Fus bac ++, mainly short forms.
(31) Yoruba. F. 15 years Domestic servant. I.P.	Commenced 5 months ago following an abrasion by a stone	Circular ulcers covering extremities of 2nd and 4th toes of R. foot. Considerable loss of tissue involving terminal phalanges. Edges everted. Base of slough covered with a thick greyish-blood-stained discharge. Foul smell. Very painful. Base of toes thickened and oedematous.	Spiros ++. Fus bac ++.	Spiros ++. Fus bac ++.

Agar culture.	Mouth.	Treatment.	Remarks.	Sheet 6.
Ps. pyocyanea. Gram + cocci.	Spiros++, a few of ulcer type. Fus bac+, scanty.	1. H.B.F. 2. Saline dressing.	General condition poor. At 4 days ulcer much cleaner, slough separating. At 7 days commenced to granulate, discharge much less copious. At 14 days healing, no spiro or fus bac seen. Patient discharged to O.P. Dept for creating disturbance. Not seen again.	
Diphtheroid bac.	Spiros+, none of ulcer type. No fus bac seen.	1. H.B.F. 2. Cyllin baths.	General condition good. At third day cleaner, discharge less. At 6th day slough separating. At 8th day granulating base. Patient did not attend for further treatment.	
Diphtheroid bac Ps. pyocyanea.	Spiros+++, some of ulcer type. No fus bac seen.	1. Ulcer scraped. 2. Iodoform.	General condition fair. Mouth shows marked pyorrhoea. After scraping raw surface purulent but no extension of phagedaenic process. At 6 days slight discharge, no spiro or fus bac seen. At 12 days healthy granulations. At 18 days healing rapidly, Completely healed in 6 weeks.	
Diphtheroid bac. Ps. pyocyanea.	No spiro or fus bac seen by D.G. or smears.	1. Local 4% neo- salvarsan, five applications. 2. Dry dressings.	General condition poor. Emaciated. Black scab formed which separated in 6 days leaving healthy granulations. Ulcer healed in three weeks.	
Diphtheroid bac. Ps. pyocyanea. Gram + cocci.	Spiros+, a few of ulcer type. No fus bac seen.	1. Local 4% neo- salvarsan after a months unavailing treatment with H.B.F., cyllin baths, picric lo- tion. 2. Dry dressings.	General condition good. Six applications of neo-salvarsan resulted in dry brown scab which separated in 4 days leaving healthy granulations. At 4 weeks when almost healed 4th toe ulcer broke down again, spiro and fus bac numerous. Four further applications of neo-salvarsan. Result as above, dry dressings after separation of scab. Completely healed at end of 10 weeks.	

Patient.	History.	Clinical appearance.	D.G.	Smears.
(32) Yoruba. F. 4 years. Nil. O.P.	Commenced 2 weeks ago following an abrasion by a fall.	Circular ulcer 1" diam on R. knee. Edges regular, swollen, rolled appearance, not undermined. Base of greyish-yellow slough covered with a thick discharge. Surrounding tissues oedematous. Foul smell. Painful.	Spiros +++. Fus bac +. Elongates +.	Spiros +++. Fus bac ++.
(33) Zabaruma. M. 25 years. Labourer. I.P.	Commenced several months ago at site of minor injury by a stick.	Oval ulcer 2½x1½" with small bud like extension at one side. Situated on anterior aspect of lower third of L. leg. Edges regular, slightly raised and thickened, not undermined. Base of ragged slough covered with a thick blood-stained discharge. Oedema and hyperpigmentation of surrounding skin. Foul smell. Remarkably little pain.	Spiros ++. Fus bac. +.	Spiros ++. Fus bac +, very pleomorphic.
(34) Hausa. M. 29 years. Labourer. I.P.	Commenced two weeks at site of a scald. The blister broke down and ulcerated.	Oval ulcer on extremity of 2nd toe of R. foot. Edges swollen, regular, not undermined. Base of slough covered with a thick blood-stained discharge. Toe much swollen. Foul smell. Not very painful. Commencing ulceration of 5th toe around nail fold.	Spiros +. Fus bac +. elongates +.	Spiros ++. Fus bac +++.
(35) Zabaruma. M. 20 years. Farmer. I.P.	Commenced about a year ago following an injury with a machet. Started to extend 2 weeks ago, when 2nd ulcer also started as a bleb.	(1). Oval ulcer 2½x1½" on anterior surface lower third of L. leg. Edges regular, slightly raised and thickened, not undermined. Base even and composed of adherent slough. Thick blood-stained discharge. Foul smell. Little pain. Surrounding skin thickened and hyper-pigmented. (2). Cottage-loaf shaped ulcer 1½x1" on posterior aspect of L. ankle. Similar to above but edges flat. (3). Collapsed bleb, just below 2nd ulcer, with sero-purulent discharge.	Spiros +. Fus bac ++. Elongates + in ulcers. Spiros and fus bac ++ in bleb contents.	Spiros +. Fus bac ++. Elongates + in ulcers. Spiros and fus bac ++ in bleb contents.

Agar culture.	Mouth.	Treatment.	Remarks.	Sheet 7.
Diphtheroid bac. Ps. pyocyanea. Gram + cocci.	Spiros+, some of ulcer type. Fus bac +.	1. Local 2% neo- salvarsan, four applications. 2. Saline dressings. 3. Acriflavine 1 in 1000.	General condition good. The treatment with local neo-salvarsan produced much irritation and a copious discharge. At 4 days ulcer increasing in size, spiros and fus bac numerous. Patient then put on saline dressings, afterwards acriflavine. Healed in about three weeks.	
Ps. pyocyanea. Diphtheroid bac.	Spiros+, scanty, a few of ulcer type. Fus bac. +.	1. Ulcer scraped and edges pared. 2. Dry dressings.	General condition poor. Raw surface after scraping remained clean. At 10 days healing rapidly. At 4 weeks when almost healed ulcer broke down, remained superficial but advanced slowly with a serpiginous edge. Various treatments tried but patient left hospital with ulcer in a stationary condition. No spiros or fus bac seen in the atypical recrudescence. Haemolytic streptococci isolated.	
Diphtheroid bac. Ps. pyocyanea. Gram + cocci.	Spiros++, some of ulcer type. Fus bac+, scanty.	1. Local 4% neo- salvarsan, eight applications. 2. Dry dressings. 3. Lotio rubra.	General condition good. Mouth shows pyorrhoea. After 4 daily applications of neo- salvarsan discharge still profuse, spiros and fus bac numerous. Four further appli- cations resulted in scab formation and drying up of ulcer. Healed slowly, 6 weeks.	
Diphtheroid bac.	Spiros++, many of ulcer type. Fus bac+.	1. Local 4% neo- salvarsan, four applications. 2. Dry dressings. 3. Lotio rubra.	General condition fair. Mouth shows pyorrhoea. At 4 days ulcer dry and black scab formed which separated at 8 days. At 3 weeks healing slowly. At 5 weeks 1st ulcer broke down in similar way to Case 33. Autogenous streptococcal vaccine prepared. Patient refused treatment and left hospital.	

Patient.	History.	Clinical appearance.	D.G.	Smears.
(36) Yoruba. F. 18 years. Fish seller. I.P.	Commenced 7 months ago following injury of old scar.	Serpiginous ulcer 3½x2", anterior aspect lower third of L. leg on an area of old scar tissue. Edges slightly raised and thickened, not undermined. Base composed of partly slough and partly septic granulations. Tibia involved. Thick blood-stained discharge. Foul smell. Very painful. Hyper-pigmentation of surrounding skin.	Spiros ++. Fus bac ++. Elongates ++.	Spiros ++. Fus bac ++, a few club forms.
(37) Hausa. M. 25 years. Nil. I.P.	Commenced 2 months ago following injury of old scar.	Oval ulcer 3x2" over mid third of R. tibia on an area of old scar. Edges a little thickened, rather irregular, not undermined. Ulcer somewhat funnel shape, base of small diam and consisting of exposed bone and septic granulations. Thick purulent discharge. Foul smell. Diffuse periostitis of tibia.	Spiros +, scanty. Fus bac. +.	Spiros +, scanty. Fus bac. +.
(38) Yoruba. M. 20 years. Labourer. O.P.	Commenced 2 weeks ago at site of minor injury.	Circular ulcer 1½" diam over L. medial malleolus. Regular, rolled edge, not undermined. Base of septic granulations with a central greyish slough. Foul smell. Not very painful.	Spiros +. Fus bac. +.	Spiros +, scanty. Fus bac ++, mainly short paired forms.
(39) Hausa. M. 25 years. Nil. I.P.	Commenced 4 days ago as an itchy spot which he scratched.	Circular ulcer 2½" diam over L. lateral malleolus. Edges flat and necrotic. Base of necrotic tissue undergoing liquefaction. Discharge thick and consisting largely of altered blood. Putrid smell. Surrounding tissues oedematous. Very painful. A fulminating type.	Spiros +++. Fus bac ++. Elongates ++.	Spiros +++. Fus bac +++.

Agar culture.	Mouth.	Treatment.	Remarks.	Sheet 8.
Diphtheroid bac. Ps. pyocyanea. Gram + cocci.	Spiros +, a few of ulcer type. Fus bac. ++.	1. Local 4% neo-salvarsan, 6 applications. 2. Neo-salvarsan injections. 3. Eusol pack.	General condition poor. Patient looks ill. Appearance of tibia suggestive of syphilis. Kahn test strongly positive. Tropical ulcer probably superimposed on syphilitic lesion. Condition improved rapidly under local neo-salvarsan, ulcer healing up except where bone involved. Injections of neo-salvarsan after local applications. Healed, except for sinus leading to bone, in 6 weeks. Broke down again later, superficial ulceration, no spirochetes or fus bac seen but Ps. pyocyanea recovered in pure culture.	
Diphtheroid bac. Ps. pyocyanea. Gram + cocci.	Spiros+, scanty, none of ulcer type. No fus bac seen.	1. Local 4% neo-salvarsan, 4 applications. 2. Eusol pack.	General condition poor. Rapid improvement under local neo-salvarsan. Surgical measures later for removal of sequestrum.	
Diphtheroid bac. Ps. pyocyanea.	Spiros+, none of ulcer type. No fus bac seen.	1. Local 4% neo-salvarsan, 11 applications. 2. Dry dressings.	General condition good. After third application of neo-salvarsan there was marked improvement, ulcer drying up and forming a brown scab. After 6th application put on dry dressings. A few days later ulcer broke down again, spirochetes and fus bac numerous in discharge. Five further applications of neo-salvarsan resulted in formation of dry scab. Healed in six weeks.	
Diphtheroid bac. Gram + cocci.	Spiros++, some of ulcer type. Fus bac. +.	1. Ulcer scraped. 2. Skin graft.	Patient well nourished but looks ill. After scraping the raw surface remained clean and free from infection. Healing was slow and a skin graft unsuccessful. At 8 weeks, when almost healed, patient left hospital at his own request.	

Patient.	History.	Clinical appearance.	D.G.	Smears.
(40) Ibo. M. 1½ years. O.P.	Vaccinated 3 weeks ago and ulcer developed on lower site.	Oval ulcer 1½x¾" lateral aspect mid third of upper arm. Edges regular, rolled, not undermined. Base of adherent slough covered with a thick yellow blood-stained discharge. Foul smell. Painful.	Spiros+, scanty. Fus bac+ ?.	Spiros+, scanty. Fus bac+, scanty, mainly short paired forms.
(41) Yoruba. M. 9 years. School boy. O.P.	Commenced one week ago at site of small abrasion.	1. Oval ulcer 1x½" on anterior aspect lower third of left leg. Edges flat regular, not undermined. Base of septic granulations covered with a thin sero-purulent discharge. Surrounding tissues oedematous. Not very painful. No foul smell. 2. Similar but smaller ulcer on posterior aspect of L.ankle.	Spiros ++. Fus bac+.	Spiros +. Fus bac++, many filamentous forms
(42) Yoruba. M. 15 years. Nil. I.P.	Commenced about 10 days ago following injury by a pointed stick.	Circular ulcer 1½"diam just above L. lateral malleolus. Edges swollen, rather irregular and undermined. Ulcer bordered by wrinkled sloughing skin. Base of ragged slough covered with a thick blood-stained discharge. Surrounding tissues very oedematous. Painful. Foul smell.	Spiros ++. Fus bac++.	Spiros ++ Fus bac++, many with globoid bodies.
(43) Yoruba. F. 12 years. Nil. I.P.	Commenced 2 months ago at site of minor injury.	Oval ulcer 3x2" lateral aspect lower third of L.leg. Edges regular, slightly raised and thickened, not undermined. Base composed of partly adherent slough and partly of septic granulations. Thick greenish blood-stained discharge. Painful. Foul smell.	Spiros ++. Fus bac++.	Spiros ++. Fus bac++.
(44) Ibo. M. 15 years. Labourer. I.P.	Commenced one month ago at site of minor injury by a piece of wood.	Oval ulcer 2x1" on dorsum of L.foot. Edges regular, rolled, not undermined. Base of slough covered with a thin blood-stained discharge. Surrounding tissues oedematous. Foul smell. Painful.	Spiros +. Fus bac+. Elongates+.	Spiros ++. Fus bac++.

Agar culture.	Mouth.	Treatment.	Remarks.	Sheet 9.
Diphtheroid bac. Gram + cocci.	Spiros,† none of ulcer type. No fus bac seen.	1. Local 2% neo- salvarsan, 6 applications. 2. Dry dressings.	Patient thin and under-developed. No scab formation with the local neo- salvarsan but discharge cleared up rapidly and healthy granulations appeared. Completely healed in 3 weeks.	
Diphtheroid bac. Gram + cocci.	No spiro seen. Fus bac+, large type.	1. Local 4% neo- salvarsan, 6 applications. 2. Dry dressings. 3. Lotio rubra.	General condition good. Dry scabs on both ulcers after 6 applications of neo-salvarsan. Healthy granulations after separation of scabs. Healed slowly, 8 weeks.	
Gram + cocci.	Spiros+++, many of ulcer type. Fus bac++.	1. 40% formalin. 2. H.B.F. 3. Acriflavine I-I000. 4. Dry dressings.	General condition fair. Mouth shows marked pyorrhoea. Black scab formed after application of formalin. Profuse discharge from under scab and inflammation of surroun- ding tissues. No spiro or fus bac seen in discharge, Gram+cocci only. Healing very slow. Patient left hospi- tal at own request at end of 8 weeks.	
Ps. pyocyanea.	No spiro of fus bac seen by D.G. or smears.	1. Perchloride of mercury I-I000. 2. Ulcer scraped and edges pared. 3. Dry dressings. 4. Lotio rubra.	General condition fair. Ulcer began to heal under perchloride dressings but broke down again and increased in size. After scraping, the raw surface remained fairly clean. Slight sero-purulent discharge. Healed very slowly, three months.	
Diphtheroid bac. Gram + cocci.	Spiros+, a few of ulcer type. Fus bac+, scanty.	1. 40% formalin. 2. H.B.F. 3. Acriflavine. IinI000.	General condition fair. Mouth shows pyorrhoea. Hard black scab formed following application of formalin. Scab commenced to separate in about 10 days, leaving septic granulations and a purulent discharge containing numerous Gram+cocci but no spiro or fus bac. Healed slowly, 10 weeks.	

Patient.	History.	Clinical appearance.	D.G.	Smears.
(45) Hausa. M. 25 years. Labourer. O.P.	Commenced 2 weeks ago at site of minor injury.	1. Oval ulcer 2x1" on anterior aspect lower third of L.leg. Edges slightly irregular, swollen, not undermined. Base of ragged slough covered with a thick blood-stained discharge. Foul smell. Not very painful. 2. Similar but small ulcer on dorsum of L.foot.	Spiros +. Fus bac+.	Spiros +, scanty. Fus bac+, mainly short forms.
(46) Yoruba. M. 13 years. Nil. O.P.	Commenced 1 month ago following a minor injury.	Circular ulcer 1" diam on dorsum of L.foot. Edges regular, rolled, not undermined. Base of slough covered with a thin discharge composed mainly of altered blood. Surrounding skin oede- matous and hyper-pigmented. Foul smell. Painful.	Spiros++. Fus bac+. Elongates+.	Spiros++. Fus bac++, many short stout forms.
(47) Zabaruma. M. 18 years. Labourer. I.P.	Commenced 1 month ago following injury by a stone.	Oval ulcer 2x1" anterior to R.medial malleolus. Edges regular, slightly thickened, not undermined. Ulcer deep and base composed of ragged slough and septic granulations. Thick blood-stained discharge. Very foul smell. Not very painful.	No spiroes seen. Fus bac++ some with globoid bodies.	No spiroes seen. Fus bac++, numer- ous filamentous forms, some with globoid bodies.
(48) Yoruba. M. 24 years. Motor driver. O.P.	Commenced one year ago?.	Oval ulcer on dorsum of 5th toe of L. foot. Regular, thickened edge. Base of septic granulations covered with a thin blood-stained discharge. Foul smell. Painful. Toe swollen and thickened.	Spiros.++. Fus bac+. Elongates+.	Spiros++. Fus bac++, very pleomorphic, club forms present.
(49) Yoruba. M. 17 years. Nil. I.P.	Commenced one month ago at site of minor injury.	Oval ulcer 3x2" on lateral aspect lower third of L.leg. Edges flat, regular, necrotic, not undermined. Base of ragged necrotic tissue covered with a thick blood-stained discharge. Surrounding parts oedematous. Very painful. Putrid smell. A typical phagedaenic ulceration.	Spiros+++. Fus bac++.	Spiros +++. Fus bac+++, mainly short forms.

Agar culture.	Mouth.	Treatment.	Remarks.	Sheet 10
Ps. pyocyanea. Gram+ cocci.	Spiros+, very scanty. None of ulcer type. No fus bac seen.	1. Local 4% neo-salvarsan, 4 applications. 2. Dry dressings. 3. Ung scarlet red.	General condition good. Dry scab formed over both ulcers after four applications of neo-salvarsan. Scabs separated later leaving granulating surface. Ulcer healed slowly, 2 months.	
Diphtheroid bac. Gram+ cocci.	Spiros+, none of ulcer type. No fus bac seen.	1. Local 4% neo-salvarsan, 5 applications. 2. Dry dressings. 3. Ung scarlet red.	General condition poor. No scab formation with local neo-salvarsan but ulcer cleared up rapidly. Completely healed in three weeks.	
Ps. pyocyanea. Diphtheroid bac.	Spiros+, some of ulcer type. Fus bac+.	1. 40% formalin. 2. H.B.F. 3. Lead acetate lotion.	General condition poor. Ill nourished. Application of formalin resulted in formation of hard scab. Surrounding tissues became very inflamed and tender. Inflammation subsided after fomenting for several days. Scab separated in 10 days and left an area of septic granulation. Healed in about ten weeks.	
Ps. pyocyanea. Diphtheroid bac. Gram+ cocci.	Spiros+, a few of ulcer type. Fus bac+, scanty.	1. Local 4% neo-salvarsan, 4 applications. 2. Dry dressings. 3. Ung scarlet red.	General condition good. Dry scab formed after four applications of neo-salvarsan. Separated later leaving healthy granulations. Completely healed in three weeks.	
Diphtheroid bac.	Spiros+, none of ulcer type. No fus bac seen.	1. Local 4% neo-salvarsan, 4 applications. 2. Picric lotion 1%. 3. Dry dressings. 4. Ung scarlet red.	General condition poor. After four applications of neo-salvarsan a dry scab formed which separated in 10 days. The granulating surface was purulent and healed slowly. No spiro or fus bac seen in discharge. Completely healed in two, and a half months.	

Patient.	History.	Clinical appearance.	D.G.
(50) Yoruba. F. 10 years. Schoolgirl. I.P.	Commenced three weeks ago at site of minor injury.	Circular ulcer 1" diam just above L. medial malleolus. Edges regular, rolled, not under- mined. Base of septic granulations covered with a thin yellowish discharge. Painful. No foul smell.	No spiroes seen. Fus bac +.

Smears.	Agar culture.	Mouth.	Treatment.	Remarks.	Sheet II
No spiroes seen. Fus bac ++.	Ps. pyocyanea. Gram + cocci.	No spiroes or fus bac seen by D.G. or smears.	1. Local 4% neo- salvarsan, 5 applications. 2. Dry dressings. 3. Ung scarlet red.	General condition good. Ulcer had been treated for three days with picric lotion prior to bacteriological examination. After five applications of neo-salvarsan a dry scab formed. Scab separated in seven days leaving a granulating surface with a scanty purulent discharge. Completely healed in six weeks.	